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VOLUME 27
JUNE, 1924

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ANTIRACHITIC EFFECT OF COD LIVER OIL FED DURING THE PERIOD OF PREGNANCY OR LACTATION *

ALFRED F. HESS, M.D., and MILDRED WEINSTOCK
NEW YORK

In view of the fact that cod liver oil has been found to be a specific in the prevention and cure of rickets both in animals and in man, experiments were undertaken to acquire fuller information regarding the scope of its activity. From both a theoretical and a clinical point of view, it seemed of value to ascertain whether, when cod liver oil is fed to pregnant animals, its active principle passes through the placenta and is imparted to the fetus. Furthermore, it seemed worth while to inquire whether the specific factor is secreted into the milk in quantity sufficient to protect the young. From a nutritional standpoint, the period of lactation must be regarded from two different points of view. The one, just referred to, considers solely the antirachitic virtue of the milk; the other takes into consideration supplementary food that the young may receive directly during this period. In this study, these two different aspects were considered by feeding cod liver oil to the lactating mother as well as directly to the young during the period of suckling. These questions were investigated as part of a more extensive study of the influence of diet on the subsequent development of rickets.

The rats used for these experiments were from our laboratory stock and were fed the standard dietary, which consisted of whole wheat, corn, bread and potatoes daily, with additions of oats, chopped beef, greens, milk, banana and cheese; an ample, although not an optimal dietary. The cod liver oil was the refined Norwegian variety which, in the past few years, has been frequently tested out in this laboratory; it titrates 35 drops to the gram. In all tests, whether of mother or of young, the oil was given by pipet and was not incorporated in the food. In the first test, a pregnant rat was given 5 drops of oil for the last twelve days, almost the latter half, of pregnancy. In due time, she had a litter of four. The fact that this litter was so small renders the protective dose of cod liver oil comparatively large. During the period of lactation, the oil was discontinued and merely the standard dietary given.

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* Received for publication, Sept. 22, 1923.

* From the Department of Pathology, College of Physicians and Surgeons.

After the usual preliminary interval of four weeks, the young were placed on rickets-producing dietaries. The accompanying table gives the details of this and the other experiments. It will be noted that two rickets-producing diets were fed; the No. 84 (Sherman-Pappenheimer) dietary, and another in which 5 per cent. of the flour was replaced by an equivalent amount of dry milk, dried by the Just-Hatmaker roller process. All four animals of this group developed rickets in the usual degree; in other words, little or no protection had been afforded the young by feeding the pregnant mother cod liver oil.

In the next three tests, cod liver oil was fed to the mother during lactation. In the first test, 5 drops was given for seventeen days, which constitutes more than half the lactating period. As the young did not develop marked rickets, the experiment was repeated, the same amount of oil being given, but fed to the mother throughout lactation, for the entire twenty-eight days. After this interval the young were weaned and placed on one or the other rickets-producing dietary. Four weeks later roentgenograms were taken, and the animals were killed for microscopic examination of the bones. These animals had rickets in a moderate degree, some showing histologic evidence of slight healing, a phenomenon not uncommonly noted in the course of active rickets. In order to obtain more definite information on this subject, a third test was carried out, the mother receiving 20 drops of oil throughout lactation. This amount of oil is exceedingly large, and had to be fed in divided doses in the course of the day. From the point of view of body weight, feeding the mother this amount is equivalent to giving an infant about 180 c.c. daily. As has been stated elsewhere,[1] moderate rickets developed also under these conditions, indicating that the young had derived little benefit from the feeding of cod liver oil to the mother.

In the next test, oil was fed directly to the young. It was given to the little rats by means of a pipet during the latter half (fourteen days) of the suckling period. The litter consisted of eight; one half this number were fed 6 drops of oil daily; the others served as controls. Given directly in this way, cod liver oil exerted a protective action, very slight rickets developing on the standard dietary (No. 84) after the usual test period of twenty-eight days.

It is evident that this result must presuppose a mechanism whereby cod liver oil, or its antirachitic principle, can be stored in the tissues of the young. A phenomenon of this kind is complex, and depends on various factors. Above all, the factor of growth must be taken into consideration in this connection, as in all phenomena relating to the development of rickets. This applies not merely to the active stage of

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[1] Hess, A. F.; Weinstock, Mildred, and Tolstoi, E.: Proc. Soc. Exper. Biol. & Med. **20**:371, 1923.

Prophylactic Feeding of Cod Liver Oil to Rats During Pregnancy, or to Mother or Young During Lactating Period

Rat	Stock	Oil Fed During Pregnancy	Oil Fed During Lactating Period		Drops of Cod Liver Oil (35 Drops to the Gram)	Weights of Young, Gm.	Rickets-Producing Diet to Young*	Rickets		Remarks
			To Mother	To Young				Roentgenogram (28 Days)	Microscopic (28 Days)	
5205	O.	Last 12 days			5	40–40	84	Moderate	Moderate	4 in litter
5206						38–40		Moderate	Moderate	
5203						34–48	5% dry milk	Slight	Moderate	
5204						38–50		Slight (healing?)	Moderate	
5000	O.		Last 17 days		5	48–50	84	Slight	Slight	8 in litter
5001						44–50		Moderate	Slight	
5002						46–50		Very slight	Slight	
5003						52–44		Slight	Slight	
5004						48–60	5% dry milk	Moderate	Slight	
5005						52–64		Moderate	Slight	
5006						48–58		Moderate	Slight	
5007						48–54		Moderate	Slight	
5252	O		Entire 28 days		5	30–44	84	Marked	Moderate (slight healing?)	10 in litter
5253						34–50		Marked (healing)	Moderate (healing)	
5254						40–50		Moderate	Moderate	
5255						34–56		Moderate	Moderate (slight healing)	
5256						34–40		Slight (healing?)	Moderate (slight healing)	
5257						30–54	5% dry milk	Moderate (marked healing)	Moderate (healing)	
5258						30–54		Moderate (marked healing)	Moderate (healing)	
5259						40–54		Slight	Moderate (healing)	
5260						40–60		Moderate (marked healing)	Moderate (healing)	
5261						40–60		Slight	Moderate (healing)	
5340	O.		Entire 28 days		20	40–30	84	Moderate	Moderate	7 in litter; 2 killed at end of lactating period; inorganic P of blood was 5.2 mg.; at end of exper., 3.1 mg.
5341						42–42		Moderate (healing?)	Moderate	
5342						40–40		Moderate	Moderate	
5343						42–50		Slight	Moderate	
5344						40–40		Moderate	Moderate	
5505	G.			Last 14 days	6	20–24	84	Slight	Slight	8 in litter
5506						20–30		No	Very slight	
5507						22–20		No	Very slight	
5508						22–24		Slight	Very slight	
5501						20–28		Moderate	Moderate	
5502						20–28		Moderate	Moderate	
5503						20–32		Moderate	Moderate	
5504						22–30		Moderate	Moderate	

* No. 84 diet is Sherman-Pappenheimer low phosphorus, high calcium dietary. In the dry milk dietary, 5 per cent. of the flour was replaced by an equivalent amount of dried milk.

rickets, as has been frequently emphasized, but also to the prerachitic stage. For example, in our experience, animals that have grown exceedingly rapidly during the period preceding the test subsequently develop rickets more readily than animals that have grown but slightly or moderately—the result of a storing in the tissues of the animals in which growth has been tardy. This phenomenon was recently exemplified by a series of rats which were rendered excessively large by feeding an unusually liberal and varied diet throughout lactation. These rats weighed as much as 60 gm. at the age of 4 weeks, the time when they were weaned and the experimental diet begun. Rats of our stock usually weigh from 35 to 40 gm. at this age. Before the experiment was undertaken, it was thought that these exceptionally well nourished animals might prove resistant to rickets. As a matter of fact, they evinced no refractory tendency whatsoever, having apparently no reserve of the antirachitic factor on which to draw. In contradistinction to these animals, it will be noted, as shown in the accompanying table, that the rats that were fed cod liver oil during the lactating period, and were protected thereby, were not large when they were weaned and placed on the rickets-producing dietary. The protection afforded by cod liver oil must be regarded not as an absolute factor but as one which bears a reciprocal relationship to the growth of the body. Its active principle is stored only when the oil has been taken in quantities exceeding the immediate demands of the body, and, on the other hand, is entirely consumed when the growth ratio has been excessive.

These experiments are not to be interpreted as indicating that the subsequent development of rickets in the young is not influenced by the diet of the mother during the period of pregnancy or lactation. Experiments recently published from this laboratory show that such was not the case.[2] Tests of this nature involving, necessarily, two generations are most complex, depending on various nutritional factors. An adequate discussion of this subject would lead too far afield and will be postponed until other aspects are considered.

Korenchevsky,[3] who has carried out a large number of experiments in this field of investigation, came to the conclusion that cod liver oil was of antirachitic value when given to the mother during pregnancy or lactation. It is difficult to compare the two series of experiments as he gave calcium in addition to cod liver oil. Furthermore, the nutritional condition of the animals, depending on the stock, on the nature of the standard dietaries and on other factors, renders it impossible to correlate experiments of this nature.

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[2] Hess, A. F.; Weinstock, Mildred, and Tolstoi, E.: J. Biol. Chem. **57,** No. 3, 1923.

[3] Korenchevsky, V.: Medical Research Council, Special Report, No. 71, 1922.

SUMMARY

Our experiments indicate that cod liver oil, when given to the mother during pregnancy, cannot be relied on to protect the offspring from rickets. Furthermore, the active principle of the oil is not excreted in the milk in adequate amount; rats receiving even large doses of cod liver oil were unable to afford protection to their young, which were subsequently placed on rickets-producing diets.

On the other hand, cod liver oil did confer subsequent protection when fed to the young during the latter half of the lactating period directly and not through the medium of the mother's milk, demonstrating the essential difference between direct and indirect nutrition. This protective power suggests that the specific factor in the oil can be stored by the young and drawn on in time of need. Although it cannot be taken for granted that these results are applicable to human rickets, it is probable that such distinction as exists is one of degree rather than of kind.

BLOOD PRESSURE IN THE NEW-BORN *

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Physiology and pathology approach each other so closely in obstetrics that it is often difficult to distinguish the one from the other. In fact, there are two groups of obstetricians, the one typified by Eden,[1] who considers pregnancy and parturition essentially physiologic; the other, by DeLee,[2] who considers all labor abnormal. Between these extremes, there is a large group that considers the pregnant woman to be just on the dividing line between the normal and the abnormal, usually on the normal side, but often, with the least provocation, getting over the line into the abnormal.

This condition of affairs is equally true of the new born, as one readily realizes in studying the causes of death of infants at birth and shortly thereafter. In Williams' classic study of infant deaths,[3] the next to the largest class of etiologic factors was the unknown (18 per cent.). If to these there be added other groups in which necropsy revealed no definite cause for death, i. e., prematurity (7.1 per cent.), inanition (3.3 per cent.) and debility (0.7 per cent.), we have a group that comprises 29.1 per cent. of the stillbirths and neonatal deaths, which is larger by 2.5 per cent. than Williams' first group. Thus, it will be seen that, in almost 30 per cent. of his 705 deaths, necropsy failed to reveal a satisfactory explanation. Holt and Babbitt,[4] in a study of 10,000 deliveries in the Sloane Hospital for Women in New York, found that 58 per cent. of the deaths of infants in the first two weeks were due to congenital weakness and atelectasis. "Except for the larger rôle played by syphilis, the causes of stillbirth in no way differ from those which produce death during the first days of life." Of 200 stillbirths and neonatal deaths at the Royal Maternity Hospital at Edinburgh, Browne [5] found that 40 per cent. were due to asphyxia.

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* Received for publication, Oct. 31, 1923.

[1] Eden, T. W.: Maternal Mortality of Child-Bearing, Lancet **2**:998, (Nov. 11) 1922.

[2] DeLee, J. B.: Prophylactic Forceps Operation, Am. J. Obst. & Gynec. **1**:34 (Oct.) 1920.

[3] Williams, J. W.: Limitations and Possibilities of Prenatal Care, J. A. M. A. **64**:95 (Jan. 9) 1915.

[4] Holt, L. E., and Babbitt, Ellen C.: Institutional Mortality of the New-Born, J. A. M. A. **64**:287 (Jan. 23) 1915.

[5] Browne, F. J.: Still-Birth: Its Causes, Pathology and Prevention, Edinburgh M. J. **27**:153, 199 and 286, 1921.

When the cause of death is determined largely on clinical data, as in Moran's[6] series or in the Mortuary Reports, the inanition and unknown class is even larger. On the other hand, had the newer methods of opening the cranium, such as that of Beneke,[7] the importance of which is so stressed by Ehrenfest,[8] been used, it is possible that the unknown class of Williams and Holt and Babbitt might have been smaller. Even with this possible deduction, it is evident that what we might term "physiologic" death, or death with no discoverable pathologic condition, ranks high among the causes of infant mortality.

The magnitude of the question of infant mortality was pointed out by Foote[9] in a recent editorial. "It is appalling, therefore, to realize that probably 8 per cent. of the 2,500,000 children born annually in the United States will pass away within a month from the time that they are born." If a large percentage of these 200,000 deaths are physiologic, or at least have no discoverable cause, then any investigation of the physiology of the new-born should be of interest, not only to the physiologist, but also to the pathologist, the obstetrician, the pediatrician and the public health worker.

THE LITERATURE

What is the normal blood pressure in new-born infants? This question presented itself to one of us in connection with a group of stillbirths that had rather a characteristic symptomatology. These infants were born, or were delivered, with considerable difficulty. They were pale and limp, and were apparently dead, except for pulsations at the apex, which continued for thirty or forty minutes. There was no obstruction in the air passages, but no respiratory movements could be started by any of the usual methods of resuscitation. Necropsy showed that our artificial respiration had inflated the lungs, at least partially, and there was no discoverable cause for death.

The question whether shock played a part in these cases at once brought up the question of blood pressure. Whatever may be the actual cause of shock; whether it be due to vasomotor exhaustion, as was suggested by W. W. Keen, S. Weir Mitchell and G. R. Moorehouse;[10] to mental emotion and bodily pain, singly or in combination;[11]

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[6] Moran, J. F.: Endowment of Childhood from the Obstetric Standpoint, J. A. M. A. **65**:2224 (Dec. 25) 1915.

[7] Beneke: Ueber Tentoriumzerreissungen bei Geburt sowie die Bedeutung der Duraspannung für chronische Gehirnerkrankungen, München. med. Wchnschr. **57**:2125, 1910.

[8] Ehrenfest, Hugo: Birth Injuries of the Child, New York and London, D. Appleton and Company, 1922, p. 27.

[9] Foote, John: The Hazardous First Month, Mother and Child **4**:28, 1923.

[10] Circular No. 6, Surgeon-General's Office, 1864.

[11] Mansell-Moullin, C. W.: International Encyclopaedia of Surgery, Revised Ed., New York, William Wood & Co., 1889, Vol. 1, p. 361.

to a reflex inhibition of the centers of the cord;[12] to fat emboli;[13] to acidosis;[14] to epinephrin exhaustion;[15] to a toxic agent developed in damaged tissue;[16] to damaged brain cells;[17] or to one of many different causes, as suggested by Mann,[18] extremely low blood pressure is the constant finding. In fact, Erlanger[19] defines "shock" as a reduction of arterial pressure to or below 50 mm. of mercury, together with other usual signs.

No one with whom we came in contact, obstetrician, pediatrician, or physiologist, could tell us what the blood pressure for the new-born should be under normal conditions, or how to obtain it in such cases as we were interested in at the time; although there have been quite a number of studies of the arterial pressure in older children, in both health and disease. Attempts to make clinical use of sphygmomanometry in children begin with Eckert[20] and von Basch.[21] Eckert measured the pressure in the temporal arteries, while von Basch used the radial. The method they employed was compression of the artery with a solid button measuring the force necessary to occlude the vessel. Seiler[22] used a Sahli modification of the von Basch instrument and compared his results with those he obtained with the Riva-Rocci sphygmomanometer, which had by this time come into general use. His results were almost identical with the two instruments. Friedemann[23] studied

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19. Erlanger, Joseph; Gesell, Robert; Gasser, H. S., and Elliott, B. L.: An Experimental Study of Surgical Shock, J. A. M. A. **69**:2089 (Dec. 22) 1917.

20. Eckert, Alexandrine: Zeitung Wratsch., 1882, quoted by Fr. Arnheim, Ztschr. f. klin. Med. **5**:376, 1882.

21. Von Basch, S.: Ueber Pulse Fühlen, Pulse Schreiben, und Pulse Messen, Arch. f. Kinderh. **5**:277, 1884.

22. Seiler, H.: Praktische Bemerkungen über den Blutdruck und über Normalwerte des Blutdruckes im Kindesalter, Cor. Bl. f. schweiz. Aerzte **40**:433, 1910.

23. Friedemann, J. H.: Blutdruckmessungen bei Diphtherie, Jahrb. f. Kinderh. **36,** 1893.

a few fatal cases of diphtheria with the von Basch apparatus. Shaw,[24] Heim,[25] Kolassawa,[26] Neu[27] and Eminet[28] made use of Gärtner's tonometer.[29] Hensen,[30] Biernacki,[31] Cook,[32] Beretta,[33] Oppenheimer and Bauchwitz,[34] Trumpp,[35] Stowell,[36] Wolfensohn-Kriss,[37] Gordon,[38] Michael,[39] Salle,[40] Kaupe,[41] Melvin and Murray,[42] and Seitz and Becker[43] used some form of the Riva-Rocci sphygmomanometer. Leitao,[44] in a comprehensive study of both artificially fed and breast-fed babies, used the Erlanger and Hooker apparatus.[45] Hill[46] used a Nicholson sphygmomanometer with the ordinary arm band folded once

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24. Shaw, H. L. K.: Arterial Tension in Childhood, Albany M. Ann. **21**:88, 1900.

25. Heim, P.: Das Verhalten des Blutdruckes bei neuropathischen Kindern, Deutsch. med. Wchnschr. **26**:320, 1900.

26. Kolassawa, Anna: La pression sanguine chez les enfants dans les conditions physiologiques et pathologiques, Arch. de méd. d. enf. **5**:421, 1902.

27. Neu, Maximilian: Experimentelle und klinische Blutdruck untersuchungen mit Gärtners Tonometer, Heidelberg, 1902.

28. Eminet, P. P.: Sphygmographie und Tonometrie bei gesunden Kindern im Alter von 7-15 Jahren, Arch. f. Kinderh. **46**:328, 1907.

29. Norris, G. W.: Blood-Pressure: Its Clinical Applications, Ed. 2, Philadelphia and New York, Lea & Febiger, 1916, p. 76.

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31. Biernacki, J.: The Essential Toxic Symptoms of Diphtheria, Brit. M. J. **2**:1787, 1899.

32. Cook, H. W.: Clinical Value of Blood-Pressure Determinations as a Guide to Stimulation in Sick Children, Am. J. Med. Sc. **125**:433, 1903.

33. Beretta, Linita: Della tensions arteriosa nei bambini sani nelle loro diverse eta., Clin. med. ital. **42**:100, 1903.

34. Oppenheimer, K., and Bauchwitz, S.: Ueber den Blutdruck bei gesunden Kindern, Arch. f. Kinderh. **43**:415, 1905.

35. Trumpp, J.: Blutdruckmessungen an gesunden und kranken Säuglingen, Jahrb. f. Kinderh. **63**:43, 1906.

36. Stowell, W. L.: Blood-Pressure in Children, Arch. Pediat. **25**:88, 1908.

37. Wolfensohn-Kriss, Fr. P.: Ueber den Blutdruck im Kindesalter, Arch. f. Kinderh. **53**:332, 1910.

38. Gordon, Lennox: The Blood Pressure in Cases of Acute Nephritis of Children, Arch. Pediat. **28**:343, 1911.

39. Michael, May: A Study of Blood-Pressure in Normal Children, Am. J. Dis. Child. **1**:272 (April) 1911.

40. Salle, V.: Ueber Blutdruck im Klindesalter, Jahrb. f. Kinderh. **73**:273, 1911.

41. Kaupe, Walter: Der Blutdruck im Kindesalter, Monatschr. f. Kinderh. **9**:257, 1910.

42. Melvin, G. S., and Murray, J. R.: Blood Pressure Estimation in Children, Brit. M. J. **1**:669, 1915.

43. Seitz, A., and Becker, Felix: Ueber den Blutdruck beim Neugeborenen, Zentralbl. f. Gynäk. **44**:1338, 1920.

44. Leitao, Mello: Pressae arterial na infancia, Arch. brasil. de med. **1**:729, 1911.

45. Erlanger, Joseph: A New Instrument for Determining the Minimum and Maximum Blood Pressures in Man, Johns Hopkins Hosp. Rep. **12**:53, 1904.

46. Hill, H. K.: A Note on Blood Pressure in Infants, Especially in Gastroenteritis, Arch. Pediat. **30**:588, 1913.

upon itself and applied to the thigh; while Judson and Nicholson[47] used a modification of the Fedde[48] pith ball attachment to make the pulsations of the artery more apparent. With a second cuff on the forearm, or leg, as the case might be, they were able to make both systolic and diastolic readings. Without this attachment, they found it very difficult to take blood pressure readings in infants. Hoobler[49] is the only one who has published graphic records of children's blood pressure. He found that readings taken on the thigh were from 10 to 15 mm. of mercury higher than those taken on the arm. The French observers Gaujoux,[50] Jarricot,[51] Koessler[52] and Balard[53] employed the sphygmometric oscillometer of Pachon.[54] Morse[55] used a Tycos sphygmomanometer.

The results have varied widely, and those investigators, Biernacki,[31] Cook,[32] Heim,[25] Kolossawa,[26] Hoobler,[56] Hill,[46] Morse and Hassmann,[55] Howland and Hoobler,[57] Gordon[38] and Hill,[46] who were interested in the blood pressure in connection with some pathologic condition of children, have felt the need of determining a normal for themselves. In this connection, Utheim[58] states: "A survey of the literature in regard to blood pressure in infancy reveals rather widely varying values for normal infants. The reasons for this are, as usual, that the methods employed have been different, examinations have been few

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47. Judson, C. F., and Nicholson, Percival: Blood-Pressure in Normal Children, Am. J. Dis. Child. **8**:257 (Oct.) 1914.

48. Fedde, N.: A Pith-Ball Manometer, Med. Rec. **78**:105, 1910.

49. Hoobler, B. R.: An Automatic Device for Reading Systolic and Diastolic Blood Pressures, Med. Rec. 80:1323, 1911; The Standardization of Blood Pressure Readings by Means of an Automatic Device for Indicating Systolic and Diastolic Pressures in Children, Am. J. Dis. Child. **4**:46 (July) 1912.

50. Gaujoux, E.: Recherches sur la tension artérielle normale chez l'enfant, Ann. de méd. et chir. inf. **12**:435, 1908.

51. Jarricot: Measure de la tension artérielle chez les enfants, Pediatrie Practique **10**:392, 1912.

52. Koessler, L.: D'oscillométrie appliquée à l'etude de la tension artérielle chez les enfants, Thèse de Paris, 1912.

53. Balard, Paul: Modifications évolutives du pouls et de la tension artérielle chez le nouveau-né dans les premier jours de la vie, étudiées par l'oscillométrie, Compt. rend. Soc. de biol. **73**:483, 1912; La tension artérielle et l'oscillométrie chez le Nouveau-Né, Gaz. d. hôp. **86**:837, 1913.

54. Pachon, V.: La mesure de la pression artérielle par la méthode des oscillations, Paris méd., 1911-1912, p. 122.

55. Morse, J. L., and Hassmann, D. M.: Effect of Cold Air on the Blood Pressure in Pneumonia, Am. J. Dis. Child. **12**:445 (Nov.) 1916.

56. Hoobler, B. R.: The Effects of Cold Air on Blood Pressure in Children and Young Adults in Various Stages of Tuberculosis, Am. J. Dis. Child. **4**:307 (Nov.) 1912.

57. Howland, John, and Hoobler, B. R.: The Effect of Cold Fresh Air on the Blood Pressure in Pneumonia of Children, Am. J. Dis. Child. **3**:294 (May) 1912.

58. Utheim, Kirsten: A Study of the Blood and Its Circulation in Normal Infants and in Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **20**:366 (Nov.) 1920.

and the selection of material has not been sufficiently careful." She adds a table for normal children of ages from one half to 28 months, based on thirty-five cases.

The question of width of the cuff is one that was stressed by Recklinghausen.[59] In the work on children, various widths have been used, varying from 5 to 13 cm. Oppenheimer and Bauchwitz [34] compared their figures with those of Eckert and Beretta. Although Eckert used an instrument of an entirely different type, her figures are very similar to those of Oppenheimer and Bauchwitz. On the other hand, Beretta who used the same kind of instrument but a wider cuff, obtained much lower results; which Oppenheimer and Bauchwitz believe is due to the difference in the width of the cuffs. Judson and Nicholson, however, found no difference in children under 8 years when cuffs of different widths were used. Wolfensohn-Kriss,[37] working in Sahli's clinic, found that the blood pressure (she recorded only the systolic) varied according to age, weight and height. She found no difference between the sexes. Salle found a variation commensurate with the age, and to a certain extent with the weight and height. In his cases, nephritic and neuropathic children had higher pressures. Michael [39] studied 128 normal children, ranging in height from 3½ to 5 feet. The systolic pressure varied from 99 to 125 mm. of mercury. She calculated the pressure in relation to the width of the arm band and the circumference of the arm, as suggested by Sallom; [60] in other words, she figured the pressure according to the number of square millimeters of surface compressed, and found that there was practically no variation in children of different heights. Faber and James,[61] in a study of 651 boys and 450 girls, found that systolic, diastolic and pulse pressures averaged the same for the two sexes in the various age groups, but that the standard of deviation was greater in the girls; that is to say, there was greater variability of all three pressures in females.

Most of the work that has appeared in the literature has dealt with children of from 6 months to 14 years of age. Trumpp [35] reports a few observations on infants with icterus neonatorum. At first, the pressure was 62. It rose to 80 in the first two days of the jaundice, and then fell to 50. His youngest patient was 2 days old when the first observation was made.

Vierordt,[62] in 1855, found the blood pressure in the larger arteries of the new-born to be 111. Neu,[27] in his inaugural dissertation, reports observations with Gärtner's tonometer on a few new-born babies. He found the pressure to be 90. Seitz and Becker [43] studied 102 new-born babies with the Riva-Rocci sphygmomanometer and the palpatory method. In only four cases were they able to obtain the pressure satisfactorily on the first day. *A priori,* they believe that the pressure should be low in infants at birth. All the factors directly concerned, feeble heart action, low peripheral resistance and small blood volume, are present in very young infants. The blood volume of the new-born is one nineteenth of its body weight, in contrast with one thirteenth in the adult. The results that they obtained in the four cases are shown in Table 1.

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[59] Recklinghausen, H.: Unblutige Blutdruckmessung, Arch. f. exper. Path. u. Pharmakol. **55**:375, 412, 1906.

[60] Sallom, A. K.: Standardization of Blood Pressure, New York M. J. **92**:620, 1910.

[61] Faber, H. K., and James, C. A.: The Range and Distribution of Blood Pressure in Normal Children, Am. J. Dis. Child. **22**:7 (July) 1921.

[62] Vierordt: Daten und Tabellen, Ed. 2, Jena, 1893.

The most comprehensive study of blood pressure in the new-born has been made by Balard [53] on forty infants. His observations were made at birth and at each subsequent hour for twelve hours, and then each day for ten days. He also recorded the temperature and pulse at the same time, and the daily weight. His chart shows that there was a steady rise in both systolic and diastolic pressure, while there was a marked drop in both the temperature and pulse in the first hours of life. The minimum was reached in the seventh hour, after which time there was a rise in both temperature and pulse, but not so rapid as the fall. In 1921, Balard [63] again reported forty cases and reproduced the same chart. He believes that the oscillatory method is the only practical one for very young subjects. Failure to recognize this accounts for the fact that there have been so few studies of the arterial pressure in the new-born. He quotes Mensi as having found the systolic pressure for new-born jaundiced babies to be 85 and Popoff, with the Riva-Rocci instrument, to have found the systolic pressure 70 and the diastolic 40, for babies born at term. He prefers to make his observations on the arm, because the pulsations in the brachial artery are larger and the shape of the arm is more suitable for the application of the cuff. The rubber bag in his arm band measured 6 by 13 cm.

TABLE 1.—*Blood Pressure of Young Infants (Seitz and Becker)*

Case	1st Day	3d Day	5th Day	7th Day	10th Day
A	45	55	55	60	62
B	48	60	62	60	76
C	..	54	60	63	68
D	45	52	52	58	63

METHOD

At the beginning of our work, we encountered difficulties that we later found to be the experience of everyone who has attempted to take the blood pressures of very young infants. It might be said that we had practically completed our observations before we found any literature on the subject, so that our results are entirely unbiased by any previous work. It is practically impossible to feel a new-born baby's pulse at the wrist. Seitz and Becker [43] were able to obtain it in only four out of 102 cases. While the auscultatory method is applicable in more cases, even this is uncertain and often impossible in very small infants. Hill [46] was unable to obtain readings on several infants even as old as 5 months. Hoobler [49] found it difficult to obtain blood pressure readings in children with the customary apparatus, and devised a special attachment to overcome this difficulty. He used both the arm and the thigh, and found the thigh readings to be from 10 to 15 mm. of mercury higher than those for the arm. Hensen [30] also noted that the thigh gave higher readings. Balard thinks that the oscillatory method is the only one that is clinically applicable to very young infants. In speaking of the instrument that he used, Pachon's oscillometer, Norris [64] classifies it as the most accurate aneroid instrument at present available. He quotes Bachmann's figures to show that in adults the systolic pressure is higher by 20 or 30 mm. when read by the Pachon instrument than when determined by feeling the pulse at the wrist. The oscillometer is very delicate, and with it Balard [65] has been able to demonstrate pulsations in apparently dead babies whose systolic blood pressure was only 10 mm. He has been successful in taking blood pressures in an infant that weighed only 950 gm.

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[63] Balard, Paul: La tension artérielle et l'oscillométrie chez le nouveau-né, Nourrisson **9**:304 (Sept.) 1921.

Table 2.—*Variations in Mercury Column and Sphygmomanometer Readings*

Mercury Column	Tycos Sphygmomanometer
20	22
30	32
40	42
50	52
60	61
70	70
80	80
90	88
100	99
110	108

For our work, we have used the arm entirely. The arm band was made by sewing a Barnes bag 4 cm. wide between two layers of sateen in imitation, on a reduced scale, of the arm band supplied with the Tycos sphygmomanometer. The two openings were obtained by putting a Y-tube in the stem of the Barnes bag. An effort was made to show the pulsations of the brachial artery with a Marey tambour and a

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64. Norris, G. W.: Blood Pressure, Ed. 2, Philadelphia, Lea & Febiger, 1916, p. 108.

65. Balard: Paul: L'oscillométrie de Pachon, critère de la persistance de la circulation dans la mort apparente du nouveau-né, Presse méd. **21**:*252*, 1913.

kymograph, but the amplitude of the pulse wave was too small and the inertia of the apparatus was too great. We obtained only a downward-sloping straight line as the pressure in the cuff was slowly released. However, the needle of the Tycos sphygmomanometer showed the pulsations plainly, especially the instrument with the 6 inch dial. Schrump and Zabel[66] emphasize the importance of applying the arm band snugly, and with the small capacity of the bag that we have used this is very necessary. It is quite important that the babies be quiet, as muscular contractions of the arm obscure the pulsation of the artery. Any effort to hold the arm still is resisted, and this makes it difficult to obtain an auscultatory reading. The arm band is adjusted to the bare arm and the baby is covered with a blanket. If he does not become quiet in a few minutes, he is given a bottle of sterile water, which usually appeases him. A few observations were made with the baby at the breast. The readings were repeated several times, and whenever it was possible readings were also made by the auscultatory method. The first distinct pulsation of the needle was taken to indicate the systolic pressure, and the point at which the amplitude of the pulsations diminished, the diastolic pressure. The same instrument was used in all the observations. It was checked against a mercury column with the results shown in Table 2.

MATERIAL

The material was supplied by the wards of the Memorial and St. Philip's hospitals, and for permission to use it in this study we are indebted to Professor Baughman. Supplementary material was obtained from the private practice of one of us. About one third of the subjects were negroes. Roughly speaking, the cases fall into two equal groups, which were studied independently by one or the other of us. Neither of us knew the other's results until the work was practically complete. There was no appreciable difference in the two groups. In order to make the comparison of the oscillatory and the auscultatory methods more complete, observations were made on a few older infants in the baby wards.

ANALYSIS OF RESULTS

Our results are shown in detail in Tables 3 to 6 and the accompanying charts. Babies of mothers with hypertension or toxemia were excluded from Tables 5 and 6, and do not figure in the arithmetical means. The two races were separated for two reasons: (1) we wished to see if there were any difference in the blood pressures in the newborn of the two races, and (2) the well-known difference in size of white and negro babies at term presented an insurmountable difficulty in arrangement of tables when the cases were arranged in the order of their maturity as indicated by the total length in centimeters. Table 4 is a comparison of the oscillatory method with the auscultatory method for different days of early infancy. The oscillatory readings are placed above the auscultatory results in the appropriate columns. It will be noted that the findings by the auscultatory method are generally a few millimeters of mercury lower, and that often there is a little uncertainty about the results, as we have indicated by "?".

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[66] Schrump, P., and Zabel, B.: Ueber die auskultatorische Blutdruckmessung, München. med. Wchnschr. **56**:704, 1909.

The arithmetical averages for the fifty-two normal infants are as follows: first day, 55/40; second day, 58/41; third day, 54/39; fourth day, 58/42; fifth day, 60/42; sixth day, 63/43; seventh day, 61/44; eighth day, 63/44; ninth day, 64/43, and tenth day, 64/41. This is shown graphically by Chart 1, which is that of a representative case, and by Chart 2, which is a composite chart based on the foregoing averages. These figures are somewhat higher than those of Seitz and Becker, and a little lower than Balard's, as Table 3 shows.

Table 3.—*Systolic Blood Pressure in Infants*

	Age											
	Days								Years			
Observers	1	2	3	4	5	10	15	30	½	1	2	4
Seitz and Becker	43	48	55	56	58	66	70	82	..	..	..	..
Balard	55	60	60	65	65	75	..	..	..	..	..	..
Rucker and Connell	55	58	54	58	60	64	..	..	..	..	..	..
Beretta	..	65	..	58	..	61	72	75	..	..	..	..
Trumpp	..	..	62	..	80	50	..	60	(jaundiced babies)			
Koessler	..	..	..	..	70	..	..	..	..	..	..	..
Utheim	..	..	..	..	..	..	80	85	90	100	100	..
Leitao	..	..	..	..	..	..	..	66	73	80	87	99
Cook	..	..	..	..	..	..	..	70	82	..	..	..
Oppenehimer and Bauchwitz	..	..	..	..	..	..	..	..	80	90	90	..
Gordon	..	..	..	..	..	..	..	..	71	73	80	83
Kolassawa	..	..	..	..	..	..	..	..	..	80	..	..
Eckert	..	..	..	..	..	..	..	..	..	..	97	100
Seiler	..	..	..	..	..	..	..	..	..	..	80	83
Stowell	..	..	..	..	..	..	..	..	..	..	..	89
Kaupe	..	..	..	..	..	..	..	..	..	..	..	86
Wolfensohn-Kriss	..	..	..	..	..	..	..	..	..	..	..	85
Judson and Nicholson	..	..	..	..	..	..	..	..	..	..	..	91

The cases that we have grouped as abnormal are interesting, although they are too few to warrant any conclusions.

REPORT OF CASES

Case 1 (Chart 3).—A boy, white, 47 cm. long and weighing 2,270 gm., who was delivered by breech extraction after administration of pituitary extract had proved ineffectual, was apparently normal at birth. On the third day, he had a shrill cry, twitching of the eyelids, deviation of the eyes to the left and a rotation of the head strongly to the left. The child refused to nurse. Kernig's sign was absent. Lumbar puncture was refused. The child died the morning of the fourth day. Necropsy was not obtainable. We postulate this as a case of intracranial hemorrhage. The blood pressure, systolic and diastolic, for the first three days of life was 54, 46; 54, 46, and 88, 42, respectively.

TABLE 4.—*Comparison of Oscillatory and Auscultatory Methods**

Name	Length, Cm.	Weight, Gm.	Sex†	Race	Days									
					1	2	3	4	5	6	7	8	9	10
1. J. P.	47	2,440	♀	W	.....	.....	54/42 56/40	.....	.....	.....	.....	.....	.....	.....
2. W. W.	47	2,724	♀	C	52/22 50/24	56/24 52/30	58/38 54/36	54/38 50/38	60/40 56/40	.....	.....	.....	.....	.....
3. M. C.	49	3,248	♀	C	52/43 50/39	54/40 52/38	56/40 57/ ?	.....	56/44 55/39	.....	.....	.....	.....	.....
4. V. C.‡.........	49	3,248	♀	C	60/39 59/39	63/42 64/39	65/44 62/42	.....	.....	.....	.....	.....	70/45 68/41	66/41 62/38
5. L. P.	49	3,178	♀	C	52/39 52/43	56/39 58/41	52/38 54/ ?	55/44 52/39	61/50 54/42	63/44 56/40	62/39 60/41	68/44 64/40	64/40 60/38	67/41 65/43
6. M. M.	51	4,254	♂	C	52/39 51/ ?	52/37 51/38	52/37 48/ ?	54/40 52/39	.....	57/50 54/45	.....	.....	60/40 56/ ?	.....
7. J. J.	53	3,915	♂	C	56/40 53/ ?	60/43 56/ ?	.....	54/39 50/38	56/39 51/ ?	.....	.....	57/41 51/ ?	.....	.....
8. H. W	54	4,483	♂	C	56/36 54/39	.....	.....	56/42 56/40	.....	.....	.....	.....	.....	.....
9. P. M.	60	5,641	♂	W	64/60 62/40	62/41 63/39	64/43 62/39	62/40 64/41	.....	61/39 60/40	58/39 62/40	.....	.....	.....

* The oscillatory readings are placed above, the auscultatory below.
† In this column, ♀ indicates female; ♂, male.
‡ Preeclamptic mother.

TABLE 5.—*Blood Pressures of White Infants, Oscillatory Method*

Name	Length, Cm.	Weight, Gm.	Sex	Days									
				1	1	3	4	5	6	7	8	9	10
Mean...............	..	.....	..	54/41	61/46	54/43	56/44	61/42	62/44	62/45	63/42	67/46	64/42
1. J. S.	45	2,497	♀	40/32	.....	.....	.....	.....	.....	.....	.....	.....	.....
2. W. S.	46	2,440	♀	55/36	54/36	56/42	61/44	68/44	62/38	58/40	64/44	68/46	65/42
3. L. N.	46	2,270	♀	45/35	65/50	54/46	.....	58/48	.....	64/46	62/48	.....	.....
4. F. S.*...........	47	2,553	♂	.....	.....	54/44	.....	54/44	.....	.....	.....	.....	.....
5. J. P.	47	2,440	♂	52/44	54/44	54/42	.....	.....	.....	.....	.....	.....	52/40
6. W. B.	47½	2,851	♀	58/48	62/50	.....	.....	.....	.....	54/44	.....	.....	.....
7. I. W.	48	3,403	♂	54/36	.....	55/39	63/44	62/43	64/43	62/49	64/39	.....	.....
8. F. S.*...........	48	2,837	♂	.....	.....	49/40	.....	44/34	.....	.....	.....	.....	.....
9. I. S.	48	2,851	♀	50/42	48/40	.....	.....	54/41	.....	.....	.....	.....	.....
10. T. T.	49	.....	♂	63/42	61/40	54/40	60/40	62/44	63/41	62/39	67/44	65/38	66/40
11. J. F.	49	2,651	♂	56/44	56/38	52/40	.....	.....	.....	.....	.....	.....	.....
12. I. L.	50	.....	..	46/38	52/40	.....	.....	.....	60/48	.....	78/64	.....	.....
13. G. Y.	50	3,403	♂	52/46	48/36	.....	.....	.....	.....	.....	.....	.....	.....
14. C. J.	50	3,745	♀	64/44	66/46	.....	.....	.....	.....	.....	.....	.....	.....
15. V. P.	50	2,851	♂	54/46	62/44	.....	.....	78/64	.....	.....	.....	.....	.....
16. V. M.	50	3,178	♂	.....	.....	.....	66/48	.....	.....	.....	.....	.....	54/42
17. J. L.	50	4,303	♂	48/30	56/44	61/46	.....	.....	.....	.....	.....	.....	.....
18. C. C.	50½	3,178	♀	52/38	52/40	.....	.....	.....	.....	60/48	.....	.....	78/64
19. P. R.	51	2,894	♂	48/36	53/39	50/32	56/39	.....	.....	61/43	63/41	62/38	64/41
20. S. P.	51	2,837	♀	.....	60/40	.....	60/40	.....	56/46	.....	.....	78/48	62/44
21. M. C.	51	3,178	♀	56/44	58/44	.....	.....	.....	.....	.....	.....	.....	.....
22. W. W.	51	3,178	♀	54/40	.....	.....	.....	.....	.....	.....	.....	.....	.....
23. G. N.	51	4,086	♀	56/50	.....	.....	.....	78/60	.....	.....	.....	.....	.....
24. R. L.	52	3,415	♂	54/34	.....	.....	.....	.....	58/36	.....	.....	.....	.....
25. C. M.	52	3,745	♂	57/44	56/38	52/39	50/44	56/44	58/40	.....	62/44	61/40	70/50
26. P. S.	52	3,972	♂	58/38	.....	.....	.....	.....	.....	.....	.....	.....	.....
27. V. A.	52	3,178	♀	56/38	58/40	.....	.....	.....	.....	76/64	.....	84/70	.....
28. H. J.	52	3,461	♂	50/42	53/34	.....	.....	.....	.....	56/40	.....	.....	.....
29. J. D.	53	3,518	♂	60/40	62/48	.....	.....	.....	80/66	.....	.....	.....	.....
30. K. M.	53	3,211	♂	72/64	68/54	.....	46/40	.....	.....	.....	.....	.....	.....
31. P. M.†...........	60	5,646	♂	64/40	62/41	64/43	62/40	.....	61/39	68/39	59/45	60/42	66/44
32. K. C.	..	3,175	♂	.....	.....	.....	52/38	56/48	.....	.....	.....	.....	.....

* Twins, † Cesarean section.

TABLE 6.—*Blood Pressures of Negro Infants, Oscillatory Method*

Name	Length, Cm.	Weight, Gm.	Sex	Days									
				1	1	3	4	5	6	7	8	9	10
Mean.................	..	.....	..	55/39	55/39	54/39	57/41	56/40	60/41	60/41	62/43	62/42	64/43
1. I. M.	45	2,270	♂	48/42	50/42	.....	.....	.....	.....	.....	.....	.....	.....
2. W. W.	47	2,724	♀	52/22	56/24	58/38	54/38	60/40	66/44	62/41	61/39	64/41	63/40
3. C. W.	47	3,051	♂	56/36	54/37	58/40	60/41	.....	59/42	60/39	59/44	58/41	60/42
4. H. A.*...........	47	3,340	♂	58/40	52/39	50/36	49/39	56/40	54/38	52/41	58/44	56/40	60/44
5. D. T.	48	2,497	♂	56/38	54/40	62/38	64/34	66/48	64/44	64/46	70/50	68/46	64/40
6. M. C.	48	2,724	♀	52/43	54/40	55/40	56/40	54/41	56/44	51/44	62/40	63/40	.....
7. H. G.	49	3,340	♀	54/44	58/44	62/44	60/36	64/42	62/38	63/41	68/44	64/41	66/39
8. L. P.†...........	49	3,178	♀	54/39	56/38	52/38	53/44	61/50	63/44	62/39	68/44	64/40	67/41
9. C. B.	49	2,497	♀	62/41	56/39	58/40	57/40	60/44	62/46	70/40	.....	.....	.....
10. M. G.*...........	50	.....	♂	60/42	62/40	68/38	.....	.....	.....	68/41	.....	.....	.....
11. B. B.	50	3,440	♀	57/42	57/40	55/40	59/38	58/41	62/42	61/40	66/36	.....	64/44
12. K. D.	50	3,178	♀	56/39	52/36	.....	58/41	59/44	58/42	56/39	60/40	58/38	66/40
13. C. B.	50	3,291	♂	61/40	60/40	58/40	68/41	64/41	70/40	68/40	.....	70/42	72/42
14. A. B.	51	3,802	♂	57/41	58/41	61/42	59/42	62/40	59/44	63/40	64/50	59/41	64/42
15. C. H.	51	4,142	♂	54/38	58/44	52/39	51/40	54/38	56/38	55/41	58/49	57/44	56/45
16. M. M.	51	4,354	♂	52/39	52/37	52/37	52/38	54/40	56/40	57/40	54/38	60/40	62/40
17. G. H.	51	3,178	♀	54/39	55/44	53/38	56/38	57/38	59/41	56/46	.....	.....	.....
18. A. M.	52	.....	♂	51/40	54/39	50/40	56/42	58/39	62/39	61/40	65/36	66/36	70/40
19. J. J.	53	3.915	♂	56/46	60/43	54/40	54/39	56/39	56/41	58/39	67/44	69/44	62/40
20. H. W.	54	4,483	♂	56/36	52/38	48/36	.....	56/42	58/44	60/40	.....	68/48	70/48

* Cesarean section.

† This is the representative case shown on Chart 1.

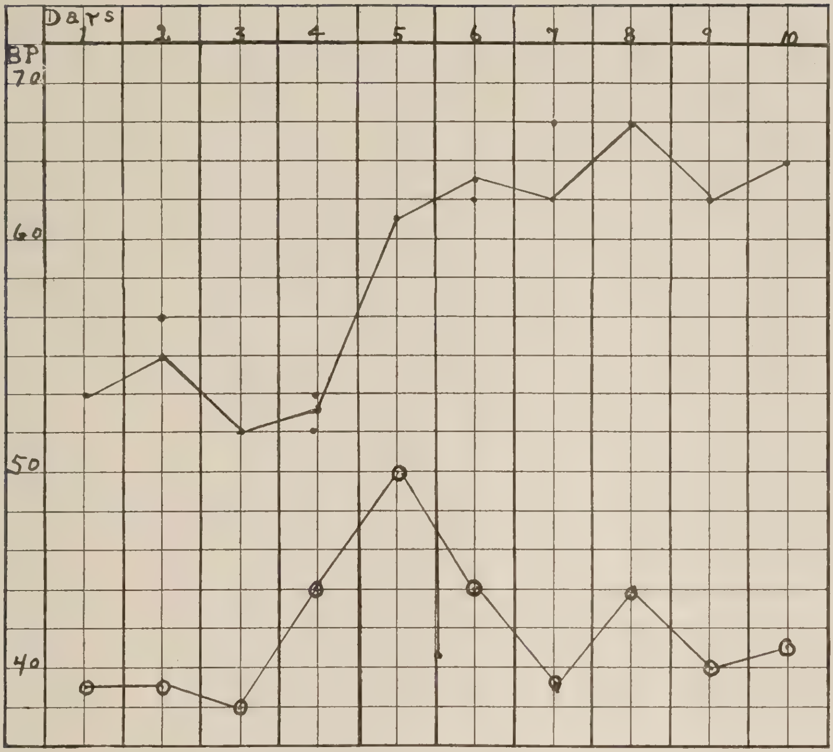

Chart 1 (L. P., colored).—Pressure curves in a representative case. In this chart and the charts following, the upper line represents the systolic, the lower the diastolic blood pressure.

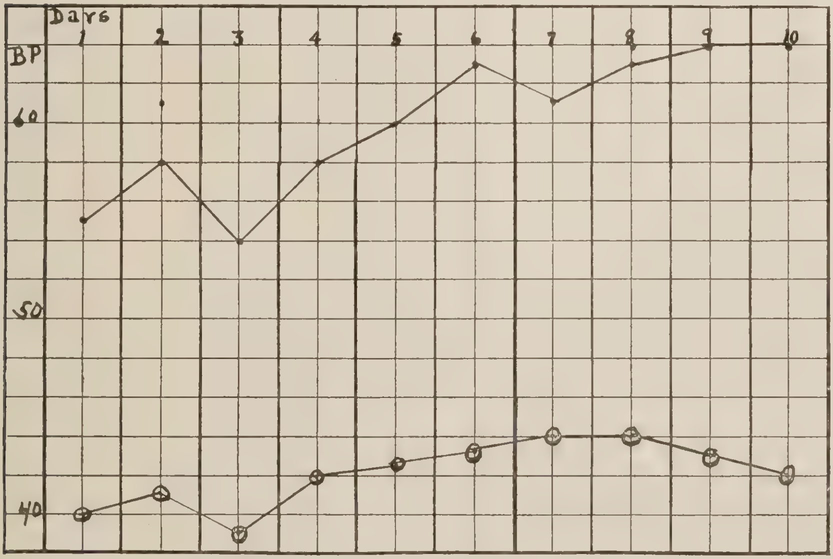

Chart 2.—Composite curves of fifty-two infants.

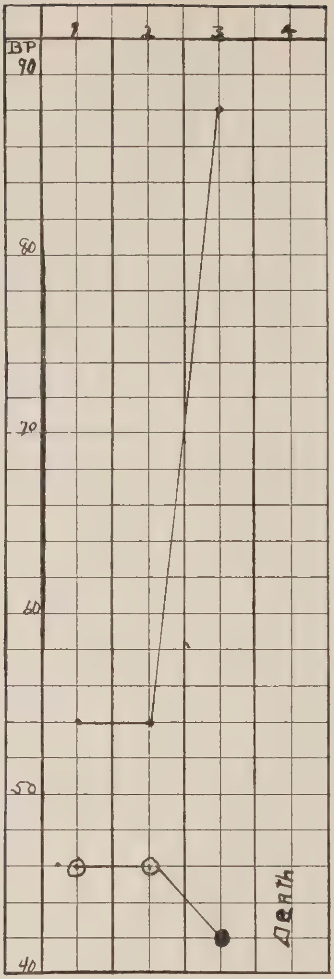

Chart 3 (Case M. W.).—Pressure curves in a case of intracranial hemorrhage (?).

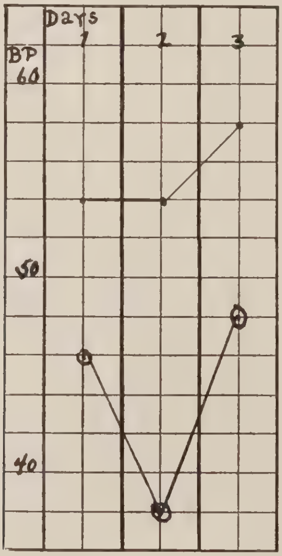

Chart 4 (Case J. W. J.).—Pressure curves in a case of eclampsia.

Case 2 (Chart 4).—A girl, white, 46 cm. long and weighing 2,270 gm., was delivered by version. The mother was in a state of eclampsia. She had three convulsions, on the day of admission to the hospital, which were controlled with morphin, gastric lavage and colonic irrigations. Two days later, her blood pressure rose from 140 systolic and 100 diastolic to 160 systolic and 110 diastolic, and she complained of severe headache. Labor was induced. Postpartum pressure was: systolic, 110; diastolic, 80. Puerperium was eventful. The baby's blood pressure, systolic and diastolic, for three days was: 54, 46; 54, 38, and 58, 48, respectively.

Case 3 (Chart 5).—A boy, white, 48 cm. long and weighing 2,610 gm., was delivered prematurely because the mother had preeclamptic toxemia. The mother's blood pressure suddenly went from 110 systolic, 60 diastolic to 150 and 100, without any other symptoms. Bread and water diet and rest in bed for a week had no influence on the blood pressure. Six hours after delivery, the blood pressure was 90 and 50. Puerperium was normal. The baby's blood pressure, systolic and diastolic, for the first, second and fifth days was 75, 55; 56, 46, and 60, 44.

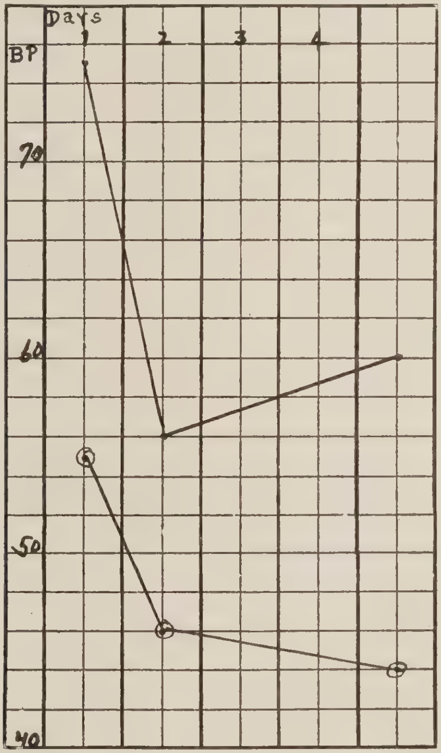

Chart 5 (Case M. P.).—Pressure curves in a case of preeclamptic toxemia.

Case 4 (Chart 6).—A girl, colored, 46 cm. in length and weighing 2,610 mg., was born of a mother who had been sent to the hospital on account of pernicious vomiting. The mother's blood pressure on admission was 179 systolic, 87 diastolic. Three hours after delivery, it was 158 and 73, and ten days later, 152 and 68. The urine and blood were normal, and the postpartum course uneventful. The baby's blood pressure, systolic and diastolic, for the first ten days was: 61, 35; 64, 36; 60, 39; 65, 43; 68, 43; 62, 42; 60, 43; 65, 44; 62, 40, and 61, 35.

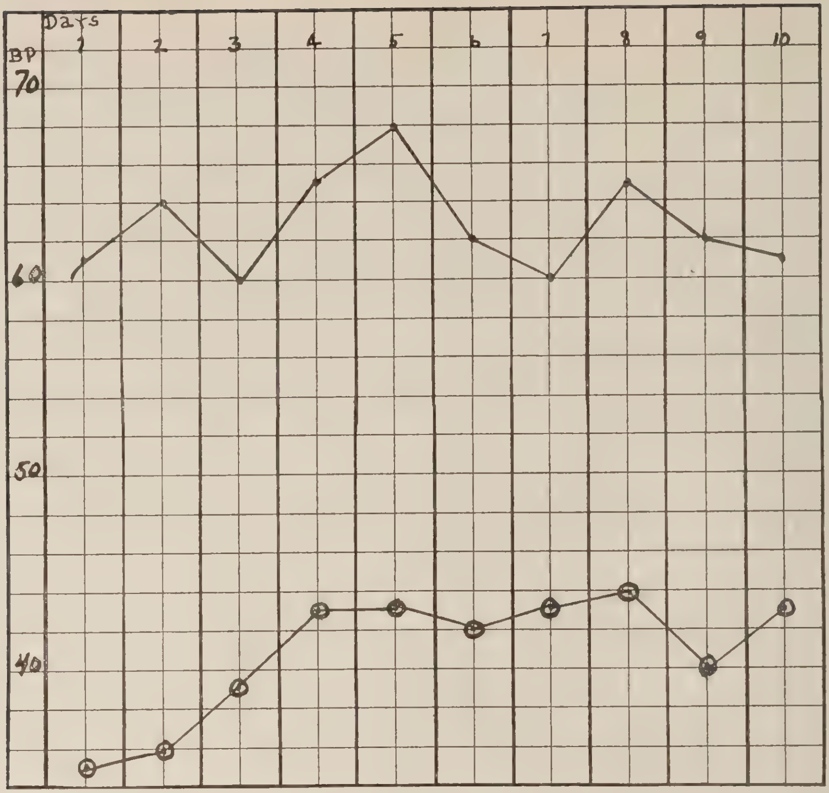

Chart 6 (Case G. F.).—Pressure curves in a case of preeclamptic toxemia.

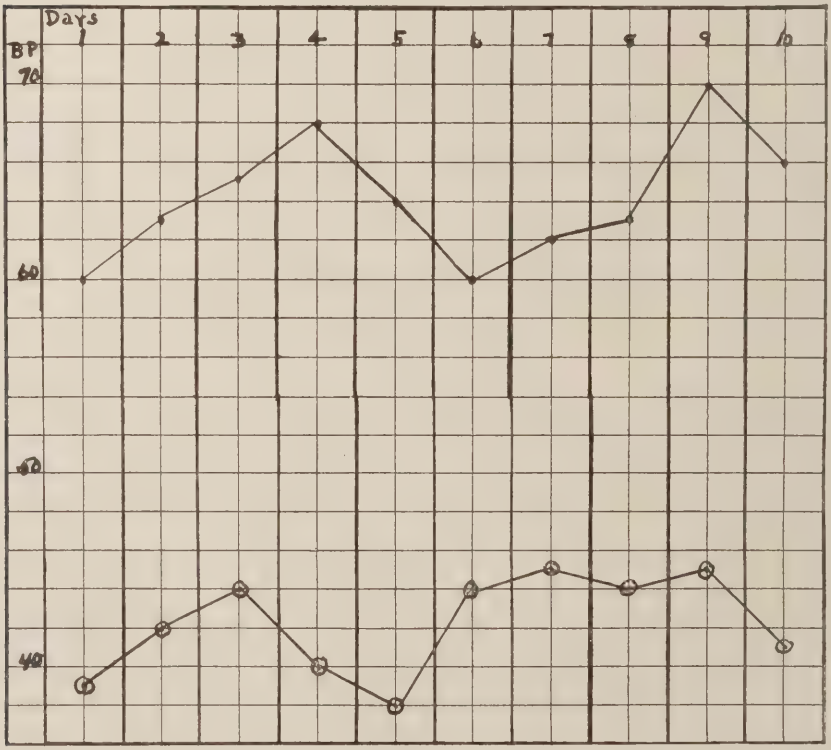

Chart 7 (Case V. C.).—Pressure curves in a case of preeclamptic toxemia.

Case 5 (Chart 7).—A girl, colored, 49 cm. in length and weighing 3,248 gm., was the result of the seventh pregnancy. The mother was preeclamptic. She was admitted to the hospital at term, but not in labor. Her blood pressure was 172 systolic, 92 diastolic on admission. She complained of headache and had edema of the ankles. Her first four pregnancies ended in abortions at five or six months. The fifth pregnancy was normal, but the sixth resulted in a still-born fetus at term. The urine contained an abundance of albumin, but no casts. Rowntree and Garaghty's test showed an excretion of 55 per cent. in two hours. The blood showed nothing abnormal. The patient remained in the hospital for ten days without going into labor. The headaches were unrelieved, but the edema was reduced somewhat by a restricted diet and rest in bed. Delivery was spontaneous at the end of a labor of twenty minutes. Postpartum blood pressure was 138 systolic, 84 diastolic, and remained at approximately this point throughout the puerperium. The baby's blood pressure, systolic and diastolic, was: 60, 39; 63, 42; 65, 44; 68, 40; 64, 38; 60, 44; 62, 45; 63, 44; 70, 45, and 66, 41.

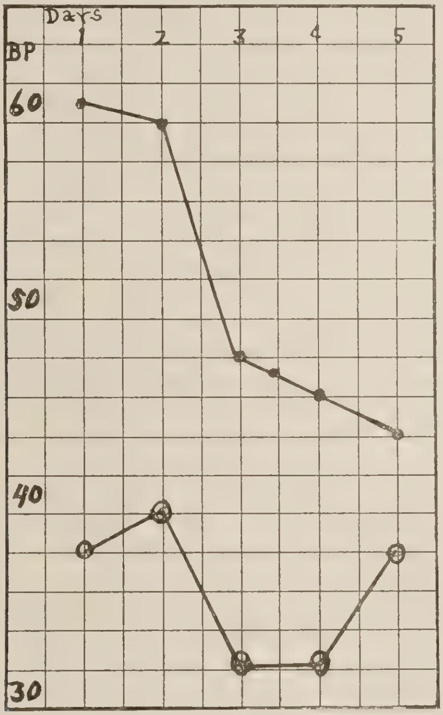

Chart 8.—Pressure curves in case of eclampsia.

Case 6 (Chart 8).—A white boy, 44 cm. in length and weighing 2,309 gm., was delivered six weeks prematurely. His mother was brought into the hospital in her eleventh convulsion, and she had two more convulsions in rapid succession. Administration of morphin, gastric lavage, colonic irrigations and intravenous glucose solution quickly controlled the convulsions. On the second day after she was admitted, the patient was conscious and it was found that her sight was so impaired that she could not see persons in the room, and could scarcely tell when the light was turned on and off. Her blood pressure, which had dropped from 195 to 135, had again risen to 175. Labor was induced. In the second stage, she again began to have convulsions. These were controlled with ether and a breech extraction was performed. Twenty-four hours later, a third series of convulsions began, lasting at intervals, when the morphin was discontinued, for four days. The baby was apparently normal, and required no resuscitation. When 2 days old, he had a peculiar crowing cry and a few slight convulsions. His blood pressure, systolic and diastolic, for the first five days was: 61, 38; 60, 40; 48, 32; 46, 32, and 44, 38.

The average blood pressure, systolic and diastolic, of the five babies in the cases reported was: 62, 45; 59, 40; 58, 41; 56, 32; 59, 41; 61, 43; 61, 44; 64, 44; 66, 43, and 64, 43. All except one of these babies were premature, and yet their blood pressures after the second day are practically identical with the averages in the normal cases. On the first day the toxic group had decidedly higher pressures. However, the group is too small to warrant our drawing any definite conclusions.

In Case 28 of our series, the patient had hemorrhagic disease of the new-born. On the second day, he vomited bright blood, and had a number of bloody stools. The hemoglobin fell to 42 per cent. He was treated with intramuscular injections, 22 c.c. of whole blood, and made a prompt and satisfactory recovery.

CONCLUSIONS

1. The oscillatory method of taking blood pressure with an aneroid sphygmomanometer is clinically applicable to new-born babies.
2. A comparison with the usual auscultatory method shows that, when used on very young infants, it is sufficiently accurate for clinical purposes.
3. The mean systolic pressure at birth is 55 mm. of mercury. The mean diastolic pressure is 40. The systolic blood pressure increases with the age of the infant more rapidly than does the diastolic pressure.
4. Toxic conditions of the mother seem to have some influence on the blood pressure of the child, which is more marked the first day of life.
5. This method may possibly furnish an additional sign of some value in the diagnosis of intracranial hemorrhage.
6. The blood pressure in general varies directly with the total length of the infant.
7. Sex shows no influence on the blood pressure of the new-born.
8. There is no difference in the blood pressure of the white and of the colored new-born infant.[67]

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[67] This article was submitted for publication before Reis and Chaloupka's article "Blood Pressure in Newborn Following Normal and Pathological Labor" (Surg., Gynec. & Obst. **37**:206 [Aug.] 1923) was published. Hence, no reference is made to their work.

BILE PIGMENTS AND BILE SALTS IN THE DUODENAL JUICE OF CHILDREN *

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Some believe that urobilin is formed only in the intestine. Others believe that, normally, it is also formed in the liver. A reabsorption from the intestine and reexcretion through the liver are both affirmed and denied.[1] It may be considered as proved that increased amounts of urobilin or urobilinogen in the stools, the urine or the duodenal juice are significant either of increased blood destruction or of hepatic disease.[2]

Ylppö examined the stools of fifty infants and found urobilin only after the second week of life.[3] Bauman states that urobilin appears in the intestine of the new-born after the third day.[4]

No reports of urobilin excretion in the duodenal juice of children have hitherto been published, but one of us (R. T.) submitted the finding of urobilinogen (600 dilution units) in the duodenal juice of a child with celiac disease as evidence of hepatic involvement. This opinion was based on Schneider's conclusion that in health more than minimal amounts of urobilinogen do not appear in the duodenal secretion.[5]

The subjects and results of the present work are shown in the accompanying table. The method was that of Wilbur and Addis as modified by Schneider, and the results are indicated as the number of dilutions, reduced to a scale of 1,000, necessary to cause the disappearance of the characteristic spectroscopic absorption bands.

Neither urobilin nor urobilinogen was found in the duodenal juice of seven infants less than 18 days old. Thirteen estimations on eight older infants showed positive results on seven occasions. There was

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* Received for publication, Sept. 17, 1923.

* From the Department of Pediatrics, University of Minnesota Medical School.

* Read at a meeting of the American Pediatric Society, French Lick, Ind., June 1, 1923.

[1] Whipple, G. H.: Physiol. Rev. **2**:440-459 (July) 1922.

[2] Wilbur, R. L., and Addis, Thomas: Urobilin: Its Clinical Significance, Arch. Int. Med. **13**:235 (Jan.) 1914; Schneider, J. P.: Anemia, Arch. Int. Med. **17**:32-39 (Jan.) 1916.

[3] Ylppö: Ztschr. f. Kinderh. **9**:208-318, 1913.

[4] Bauman: Endocrinology and Metabolism **3**:1921.

[5] Taylor, Rood: Tr. Am. Pediat. Soc. **34**:100-113, 1922.

no uniformity, the pigment being at one time present and at another absent in the same patient. The two patients with celiac disease gave findings entirely similar to those found in the younger children. There was never more than a trace of urobilinogen present.

The laws governing the formation of the chief bile salts, sodium glycocholate and sodium taurocholate, are for the most part unknown.

Bile Salts and Bile Pigments in Duodenal Juice of Children

Patient	Age	Diagnosis	Day of Experiment	Urobilinogen	Urobilin	Sodium Taurocholate, Gm. per 10 C.c. Duodenal Juice	Sodium Glycocholate, Gm. per 10 C.c. Duodenal Juice	Ratio NaT : NaGly
Os.	2 da.	Icterus neonatorum...	1	0	0	....	.....	....
Q.	4 da.	Normal...............	1	0	0	....	.....	....
Fi.	4 da.	Icterus neonatorum...	1	0	0	....	.....	....
Se.	6 da.	Normal...............	1	0	0	....	.....	....
Fo.	11 da.	Normal...............	1	0	0	....	.....	....
J.	17 da.	....	1	0	0	....	.....	....
Ry.	17 da.	Icterus neonatorum...	1	0	0	....	.....	....
P.	1 mo.	Normal...............	1	0	800	23.0	103.7	1:5
			8	0	0			
Cl.	2 mo.	Normal...............	1	0	800	11.6	83.6	1:7
			8	0	600			
			14	0	0	9.8	158.7	1:15
St.	3 mo.	Icterus neonatorum...	1	0	400	....	.....	....
H.	3 mo.	Normal...............	1	..	...	5.9	12.2	1:2
			5	..	...	9.7		
Sc.	4 mo.	Malnutrition..........	1	..	...	32.9	241.7	1:7
			21	..	...	75.9	187.3	1:2
			26	..	...	29.9	226.1	1:7
J. W.. .	4 mo.	Atrophy..............	1	..	...	21.4	156.7	1:7
			14	..	...	16.8	204.0	1:12
			19	..	...	19.8	116.3	1:6
			35	..	...	21.1	107.4	1:3
			40	0	800	39.8	163.8	1:4
Ot.	5 mo.	Otitis media..........	1	..	...	26.7	133.2	1:5
			7	..	...	17.5	48.9	1:3
			28	..	...	50.6	155.3	1:3
			37	..	...	27.6	357.0	1:13
Re.	5 mo.	Atrophy..............	1	..	...	20.9	125.4	1:6
			28	..	...	28.3	95.2	1:3
T. S. ...	7 mo.	Rickets...............	1	..	...	42.1	153.0	1:4
			8	..	...	14.2	108.8	1:8
W.	9 mo.	Normal...............	1	..	...	14.6	15.3	1:1
G.	9 mo.	Normal...............	1	Trace	800	27.6	68.0	1:2
			2	Trace	800			
Oh.	10 mo.	Normal...............	1	0	0	....	.....	....
Ca.	11 mo.	Rickets; congenital syphilis	1	0	600	....	.....	....
			3	0	0			
L.	18 mo.	Malnutrition..........	1	0	0	....	.....	....
G.	2 yr.	Celiac disease.........	1	..	...	30.1	520.0	1:17
			10	0	800			
			26	0	800	71.3	119.3	1:2
A.	6 yr.	Celiac disease.........	1	0	400	30.6	61.8	1:2
			13	0	0	37.9	202.6	1:5

Experimental work on bile fistula in dogs indicates that in health the output of bile salts varies greatly and that the output is greater on a meat than on a carbohydrate diet. It is known that there is a circulation of bile salts. They are reabsorbed from the intestine and reexcreted in the bile. To the pediatrician, they are of particular interest because they lessen intestinal putrefaction, and aid in the absorption of fat and possibly of mineral salts. Sodium taurocholate is supposed to be the more effective in lessening putrefaction.

Jacubowitsch was the first to determine the percentages of taurocholic and glycocholic acids in the bile of infants. He came to the mistaken conclusion that the percentage of taurocholic acid was the greater.[6] Baginsky and Sommerfeld, who next approached the problem, found a decided preponderance of glycocholic acid, the ratios varying from 1.5 : 1 to 13 : 1.[7] Gundobin quotes the work of Orloff and of Geptner. They found that the bile of infants contained about one-half as much bile acid as that of the adult. They also found a preponderance of glycocholic acid, although they thought it less marked than in the adult. Hammarsten's figures for the adult show a varying preponderance for glycocholic acid of from 30 : 1 to 2.25 : 1.

Determinations of bile salts in the duodenal juice have not hitherto been carried out. Specimens were collected after eight hours' fasting. All cloudy specimens containing a mixture of gastric juice were rejected. The bile acids were estimated according to the method of Schmidt and Dart.[8] Twenty-seven specimens of duodenal juice from twelve subjects were analyzed. The youngest infant was 1 month old; the oldest child, 6 years. Five were normal; three had varying grades of malnutrition, one an otitis media, one a mild rickets and two celiac disease. The results are given in the table. Wide variations in the total bile salts were to be expected and a range of from 18 mg. in a healthy infant of 3 months to 550 mg. in a 2-year-old boy with celiac disease was found.

There was a decided preponderance of sodium glycocholate; but this varied from equality to fifteen fold. There is nothing striking in the findings in patients with celiac disease. Patients J. W., Ot., Re., and T. S. were given a course of cod liver oil before the specimens were obtained, the analysis of which are shown in heavy type. No effect could be noted.

SUMMARY

The duodenal juice of infants contains a varying concentration of bile salts of from 0.2 to 5 per cent. There is a fluctuating but decided preponderance of glycocholic acid, and the content of bile salts in the duodenal juice is not influenced by the presence of celiac disease or by the administration of cod liver oil.

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[6] Jacubowitsch: Jahr. f. Kinderh. **24**:373-383, 1886.

[7] Baginsky and Sommerfeld: Jahr. f. Kinderh. **19**:321-335, 1896.

[8] Schmidt and Dart: J. Biol. Chem. **45**:415-421, 1920.

REPORT OF TWO CASES WITH UNUSUAL CALCAREOUS DEPOSITS *

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AND
I. H. ERB, M.B. (Tor.)
TORONTO

The two cases here reported present some unusual features. While they differ widely from each other in the fundamental conditions present, they have in common unusual calcareous deposits occurring in the epiphyses of some of the long bones in one patient, and in the skin and subcutaneous tissues in the other.

REPORT OF CASES

Case 1.—A boy, aged 5 weeks, admitted to the Hospital for Sick Children, Nov. 25, 1922, weighing 4 pounds and 11 ounces (2,126 gm.), was markedly emaciated and had a flexion deformity involving almost all of the joints of the body. The arms could not be elevated above the shoulders, the forearms could not be fully extended and the fingers were flexed so that, with the exception of the index fingers, they touched the palm. A slight permanent kyphosis was present. The hips, knees and ankles were also involved so that extension beyond an angle of about 135 degrees was impossible. The feet were everted and flat. All the joints appeared to be enlarged. The lower jaw was very small and receded so much that the upper lip did not approximate the lower one. These deformities are well shown in Figure 1. Examination of the muscles showed secondary contractures. A systolic murmur was heard over the precordial area.

The father and mother, who were first cousins, were quite healthy, and no history could be obtained of any similar condition occurring in any member of either family. The first pregnancy terminated at seven months, the infant being stillborn. The patient, who was the second child, was a full term infant with a birth weight of 6½ pounds (2,954 gm.). The labor was normal, and the deformities as described were present at birth. The baby did not seem able to nurse and took its artificial feeding poorly. After admission, November 25, he gradually became weaker, and died, December 26. The temperature varied from 98 to 102 F. No cause was found for the fever.

Roentgenograms were taken of the wrists, elbows, shoulders, knees and ankles. The following notes from the report of Dr. A. H. Rolph, Department of Radiology, are of interest:

"Peculiar irregular (calcareous?) deposits are present in the epiphyses at both ends of the humeri, the proximal ends of the radii, ulnae and tibiae and the distal ends of the femora. The patellae are practically outlined by these deposits. The distal ends of both radii and ulnae show a narrow zone of rarefaction just proximal to the epiphyseal lines, which is suggestive of congenital syphilis."

Unfortunately, no roentgenograms were taken of the trunk, hips or hands. The deposits were not present in the skin or muscles, or in any situation other than the epiphyses and the patellae. These deposits are shown in Figures 2 and 3.

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* Received for publication, Oct. 26, 1923.

* From the wards and laboratories of the Hospital for Sick Children and the departments of pediatrics of the University of Toronto.

A Wassermann test made with blood obtained from the patient, December 17, was negative; the blood from the mother was also negative. November 25, the red blood count was 4,750,000; hemoglobin, 85 per cent.; white blood count, 13,200, with 65 per cent. polymorphonuclear cells. December 21, the white blood count was 7,800. The intracutaneous tuberculin test was negative. The blood serum calcium, November 30, was 9.3 mg. per hundred cubic centimeters and the inorganic phosphorus, 4.5 mg.

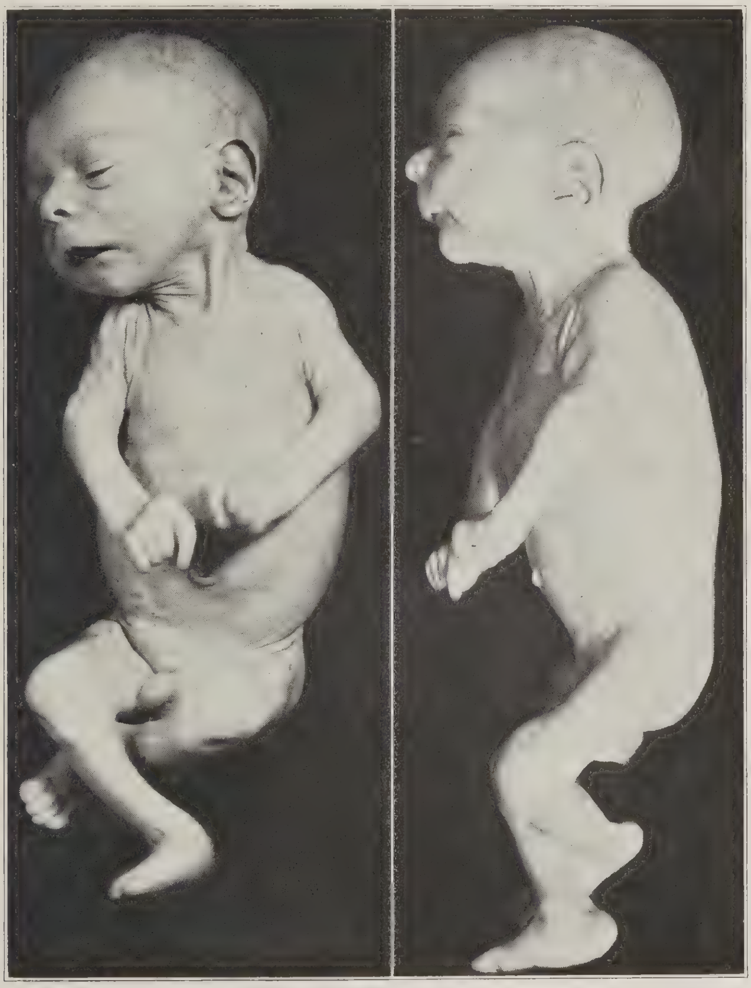

Fig. 1 (Case 1).—Front and side views of infant.

Summary of Postmortem Findings.—No gross abnormalities of the gastrointestinal tract, spleen, liver or lungs were found. The ductus arteriosus was patent, and the wall of the right ventricle of the heart was somewhat hypertrophied. The flexion deformities of the various joints, previously described, were noted. The left patella and right olecranon process were removed for further study.

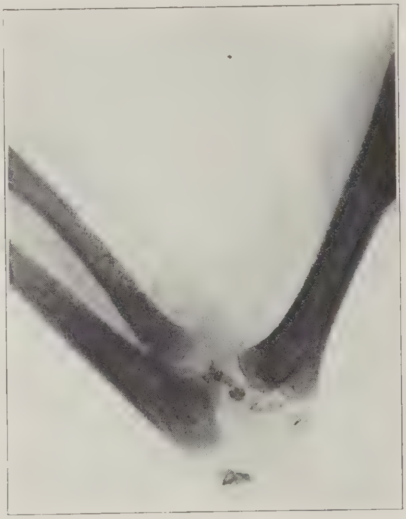

Fig. 2 (Case 1).—Left arm: Calcareous deposits in the region of the elbow joint.

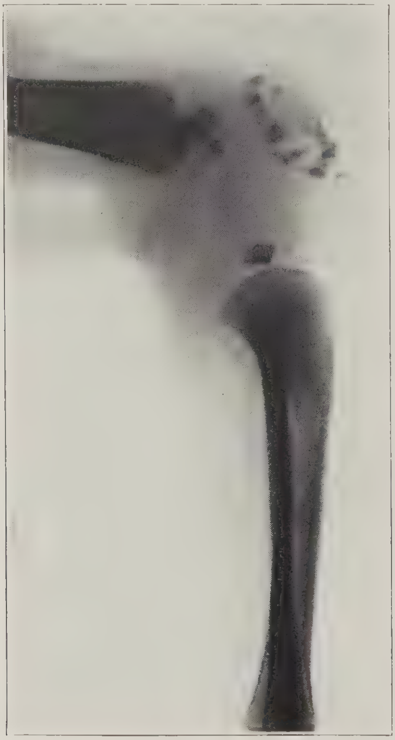

Fig. 3 (Case 1).—Left leg: Calcareous deposits in the region of the knee joint.

Microscopic examination of the various tissues revealed nothing pathologic in the thymus gland, suprarenals or pancreas. There was slight congestion of the lungs and quite marked congestion of the liver. In both the liver and the spleen were numerous Kupffer cells, showing marked phagocytosis for red blood cells. The kidneys showed marked congestion of the capillaries below the pelvic epithelium and small laminated renal calculi in the pelvis. A few of the renal tubules were dilated and filled with granular débris, in which were calcareous deposits. Examination of the patella showed that the bulk of the section was cartilaginous, but scattered here and there throughout the substance of the cartilage were areas of loose connective tissue This connective tissue was peculiar in that many of the cells appeared to be undergoing degenerative changes,

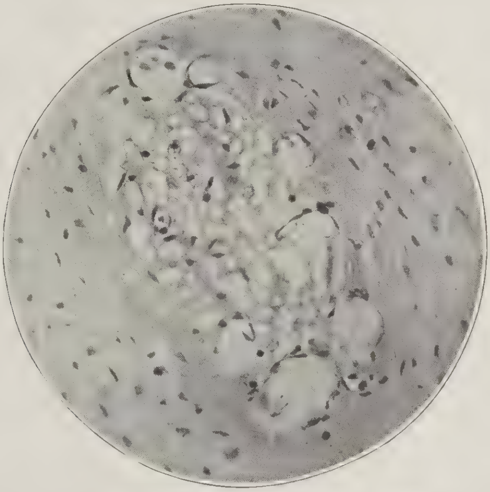

Fig. 4 (Case 1).—Photomicrograph of section of patella: Vacuolated appearance, with areas in which nuclei have disappeared.

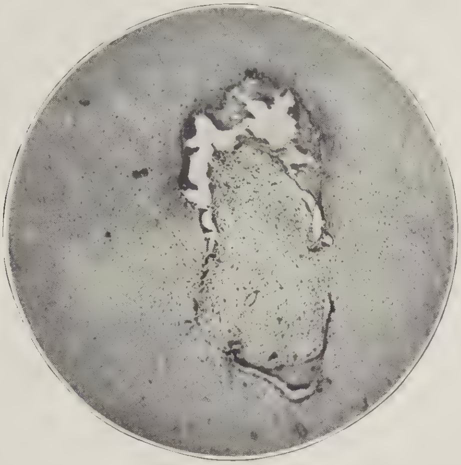

Fig. 5 (Case 1).—Photomicrograph of section of patella: Calcareous deposits in degenerated connective tissue.

some of the nuclei being shrunken and the intercellular substance vacuolated and granular. It was in these areas of degeneration that the deposits were found, the cells having entirely disappeared in some places, the space being occupied by rather dense calcareous material. This calcareous material had evidently acted as a foreign body, since an occasional foreign body giant cell was seen at the periphery of these areas. There was no other evidence of any inflammatory reaction (Figures 4 and 5). Somewhat similar areas of degeneration were seen in the connective tissue toward the base of the mitral valve curtains, but here there was no deposition of calcium salts.

Case 2.—A boy, aged 12 years, admitted to the Hospital for Sick Children, May 17, 1922, was markedly emaciated, with contracture deformities of the knees, hips and elbows. In regard to the skin, itchiness was marked. It had a pinkish tinge and presented a most unusual appearance (Figs. 6 and 7). With the exception of small areas around the umbilicus and on each side of the spinous processes, it was rough, dry and mottled. Scars of old bed sores were present over some of the vertebrae. Other small scars were present, lateral to the sacrum, on the elbows and on the legs. There were some wartlike projections on the right leg and both elbows. These consisted of calcareous material which appeared to be in the process of erosion through the skin. Some of these were removed quite readily, and areas were left which healed and formed small scars similar to the ones already mentioned. On palpation of the skin of the extremities and certain parts of the trunk, hard plaques of material were felt, varying in size from just palpable spicules to one piece which extended from the right external malleolus up the leg for a distance of about 18 cm., and was from 2 to 4 cm. in width. Examination of the glandular, respiratory, circulatory, digestive and nervous systems disclosed nothing abnormal. The family history was negative.

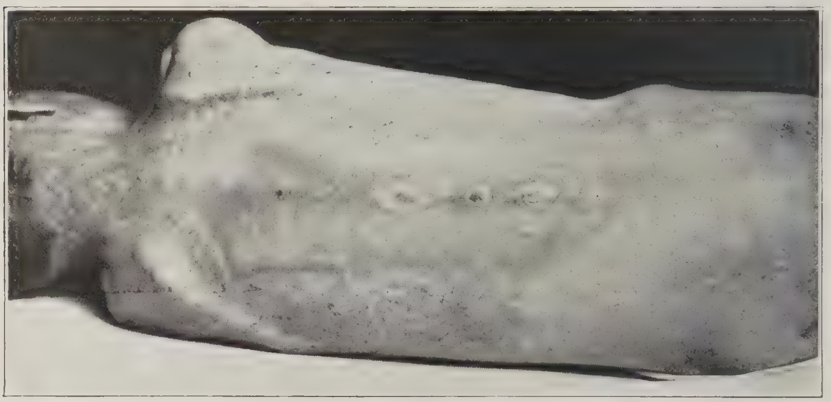

Fig. 6 (Case 2).—Appearance of patient: Unusual skin condition.

The boy had apparently been normal until May, 1918, when he complained of pain in his ankles and difficulty in walking. The father noted a small sore on the internal malleolus of one ankle. A few days later, a similar sore appeared on the internal malleolus of the other ankle. He was then brought to the hospital, and attended the outpatient department once a week for three months. At this time, he was able to walk a little, but dragged his legs as though very tired. He was admitted to the hospital in September, and discharged in December, 1918. His condition had become progressively worse, and on discharge he was unable to walk at all. The condition of the skin at that time was apparently as previously described. The contractures of the arms and legs were first noticed in the spring of 1919, and have gradually become more marked. His mentality has been excellent throughout.

Roentgenograms were taken of the extremities and the trunk. The following report by Dr. A. H. Rolph, Department of Radiology, is of interest:

"Numerous calcium deposits are present in the subcutaneous tissues of both legs and arms. These all appear to be very superficial and not in the muscles as occurs in myositis ossificans. The calcareous material is also widely distributed throughout the subcutaneous tissues of both buttocks." The accompanying roentgenograms show some of these deposits (Figs. 8 and 9).

The Wassermann reaction with the blood was negative. May 17, 1922, the red blood count was 4,150,000; white blood count, 6,200, with 78 per cent. polymorphonuclear cells; the hemoglobin, 75 per cent. The intracutaneous tuberculin test was negative. The blood serum calcium, May 25, was 9.7 mg. per hundred cubic centimeters and the inorganic phosphorus 4.4 mg.

A small nodule was removed from the skin of the right arm above the elbow for microscopic examination. This nodule showed quite normal squamous epithelium and sebaceous and sweat glands. In the subcutaneous areolar tissue was a small calcareous mass surrounded by a rather dense zone of connective tissue. The calcareous material was vacuolated, suggesting the possibility that fatty material had been dissolved out during the process of dehydration in the preparation of the tissue for section. The areolar tissue outside the nodule appeared normal.

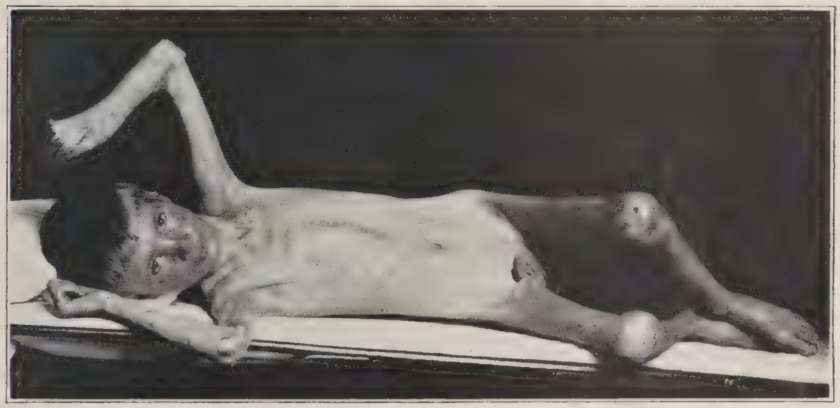

Fig. 7 (Case 2).—Appearance of patient.

COMMENT

In a careful survey of the literature, the authors have been unable to find any case similar to the first reported in this paper. The diagnosis in the second case rests between xeroderma pigmentosum and scleroderma. The following extract is from the notes made on this case by Dr. H. A. Dixon of the sub-department of dermatology:

"Xeroderma pigmentosum (pigmented dry skin) rarely begins after the second year. In the early stages, the exposed parts are involved. The changes are in order, freckle-like pigmentation, white atrophic spots and telangiectasis; later superficial ulceration occurs, and this may be followed by warty growths, malignant epithelioma and a fatal issue.

The ulcers are due to secondary infection and are followed by contractures. The affected skin is especially sensitive to the actinic ray of sunlight and even slight exposure may set up a solar dermatitis.

"Scleroderma (hard skin) when becoming generalized is slowly progressive and may be subject to periods of intermission, months and even years elapsing before it reaches the final stages. Occasionally after a stationary period, the skin may gradually return to normal. Owing to the atrophy, the subcutaneous fat disappears and the skin becomes bound down to underlying structures. The knees and elbows may become so fixed that flexion is impossible. The vitality of the

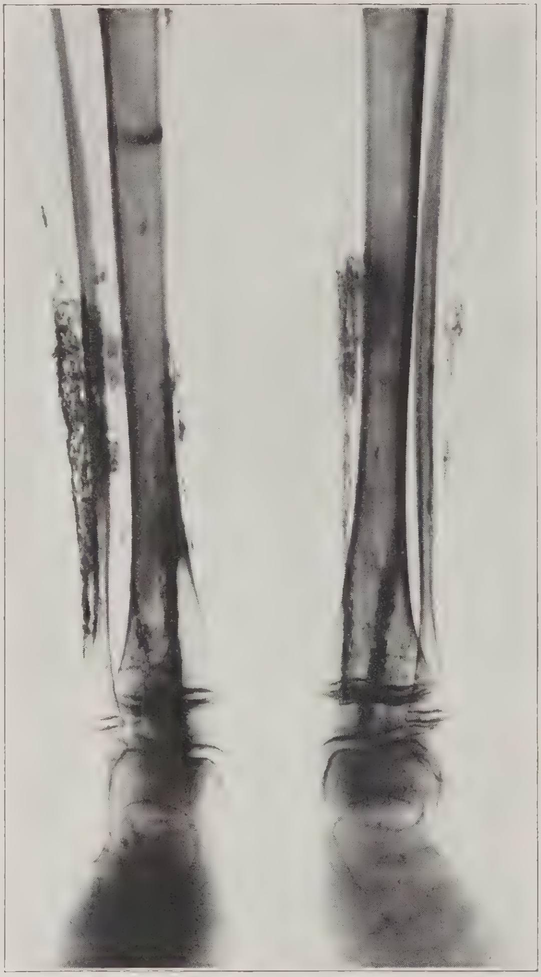

Fig. 8 (Case 2).—Calcareous deposits in the skin and subcutaneous tissues (legs).

skin is so low that slight injury, especially about the prominent parts, such as the elbows, knees and malleoli, may give rise to ulceration and even gangrene. The later phases of the fibrosis may lead to calcareous deposits of calcium phosphate and calcium carbonate.

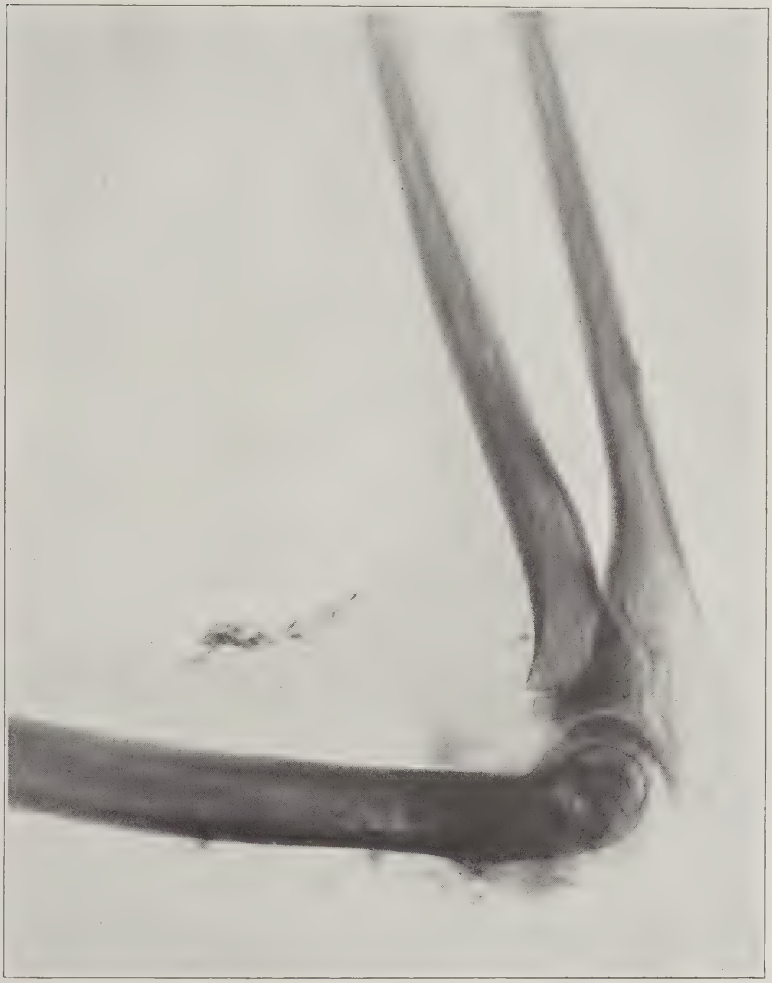

Fig. 9 (Case 2).—Calcareous deposits in the skin and subcutaneous tissues (left arm).

"The present case shows very marked contractures and areas of atrophy and pigmentation. Definite calcareous deposits are also present. In our opinion, this case very closely resembles xeroderma pigmentosum, but in a review of the literature we have been unable to find any records of calcareous deposits in the skin in this disease. On the other hand, there have been reported a few cases of scleroderma with calcium deposits in the skin, and on this account the weight of evidence is on the side of the latter disease."

The occurrence of calcareous deposits in the skin and subcutaneous tissues has been noted by a number of authors. It is not limited to any one disease. Morse [1] has recently reported an unusual instance of necrosis of the subcutaneous fat in a 3½-year-old girl, which was followed by calcification. Calcareous deposits in the subcutaneous tissue in cases of scleroderma, as already mentioned, have been reported by Hunter [2] and others. Kuznitzky and Melchior [3] have described calcareous deposits in the skin in an atypical case of lipodystrophia progressiva. Under the heading "Ueber Kalkmetastasen in der Haut," Jadassohn [4] reported a case of a 12-year-old boy who had calcareous deposits not only in the skin, but also in the endocardium, lungs and kidneys. This patient had an osteomyelitis of the pelvic bones, and shortly before death staphylococci were obtained from the blood stream. Raynaud's disease may apparently be a factor in the subcutaneous deposition of calcium salts.[2] The presence of calcium in the skin and subcutaneous tissues in a case of leukemia has been noted by Riehl.[5] Also, a number of German authors have reported the occurrence of calcareous deposits in the skin which did not follow any particular disease. These deposits occurred chiefly in the region of the phalangeal joints, along the course of the ulna and at the elbow; and although they are not limited to any one disease, the microscopic findings in the different conditions are almost identical. Inflammatory changes are not a factor in these deposits. In the early stages of calcification, it is unusual to find round cells or giant cells, although in the later stages these calcareous masses may act as foreign bodies and produce some mechanical irritation. The majority of authors have found that the deposition occurs in or around degenerated tissue cells. Jadassohn, however, observed in his case that there was no degeneration of the elastic or connective tissue fibers at the site of some of the recent calcareous deposits. Nevertheless, he considered that probably a toxin had diminished the vitality of these cells, and that this in some way favored the deposition of the calcium salts. Practically all the writers are of the opinion that the deposits do not occur in normal tissue cells.

Under the name of myositis ossificans progressiva, a number of cases have been described with calcareous deposits in the muscles. In

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1. Morse, J. L.: Calcification of Skin in a Child, Am. J. Dis. Child. **22:** 412 (Oct.) 1921.
2. Hunter, W. K.: Glasgow M. J. **79:** 241, 1913.
3. Kuznitsky, E., and Melchior, E.: Arch. f. Dermat. u. Syph. **123:** 133, 1916.
4. Jadassohn, J.: Arch. f. Dermat. u. Syph. **100:** 317, 1910.
5. Riehl: Arch. f. Dermat. u. Syph. **117:** 299, 1913.

this condition, the deposits occur not in normal muscle tissue but in a fibrocellular connective tissue which invades the normal muscle and connective tissue cells. This new formed tissue is not the result of any inflammatory change, but is rather a simple hyperplasia of unknown origin.

It is a matter of common experience to find calcareous deposits in various tissues in which there have been degenerative changes. For example, calcareous tubercles in the lung, in the cervical, bronchial or mesenteric glands, are frequently seen. Calcareous plaques in the aorta and other arteries in arteriosclerosis are quite common. Less frequently seen, but still fairly common, are the calcareous deposits in necrotic renal epithelium in some cases of marked nephrosis. Occasionally, one meets with similar deposits in inspissated pus in an old empyema. In fact, one such case recently seen by one of us (I. H. E.) showed a thick layer of calcareous material over the lung at the left apex, at one point of which there was in addition actual bone formation. In all of the above mentioned conditions, the calcification is preceded by degenerative changes, the fatty, necrotic material evidently favoring the deposition of calcium salts.

In the light of these facts, the microscopic appearance of the tissues involved in the cases here reported is of considerable interest. In Case 1, the areas of connective tissue in the patella show numerous vacuoles of various sizes with comparatively few nuclei remaining. This is best illustrated in Figure 5. Figure 6, which is from the same case, shows what appears to be a more advanced stage in the degenerative process, with fairly heavy deposits of calcium in the region of the connective tissue. Quite similar findings are seen in the nodule removed from the skin in Case 2, except that numerous vacuoles are still present in the calcareous areas. It would thus appear that while these two cases present very different clinical pictures, the calcareous deposits in both cases occurred in areas showing previous degenerative changes.

On account of the importance of the concentration of the blood serum calcium and inorganic phosphorus for the deposition of bone in healing rickets [6] and also in the union of fractures,[7] the concentration of these elements was determined in the serum of both cases. The values obtained were within the normal limits, although rather less than the average (average calcium per hundred cubic centimeters of serum, 10.0 mg.; average inorganic phosphorus value per hundred cubic centimeters of serum in children, 5.0 mg).

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[6] Howland, John, and Kramer, Benjamin: Calcium and Phosphorus in Serum in Relation to Rickets, Am. J. Dis. Child. **22:** 105 (Aug.) 1921.

[7] Tisdall, F. F., and Harris, R. I.: Calcium and Phosphorus Metabolism in Patients with Fractures, J. A. M. A. **79:** 884 (Sept. 9) 1922.

The only previously recorded determinations of the calcium concentration in the blood of a patient with subcutaneous deposits of calcium are those reported by Mosbacher,[8] in 1918. He placed his patient on a diet with a low calcium content, then on a diet with a high calcium content. On the first diet, he obtained a value of 18 mg. calcium per hundred cubic centimeters of blood; and on the latter, a value of 43 mg. However, his determinations of the blood calcium in a normal individual under the same conditions were 17 and 28 mg. of calcium per hundred cubic centimeters, respectively. In view of the known constancy of the calcium concentration in blood serum of normal individuals, it is obvious that no importance can be placed on these determinations.

The results of our investigations throw no further light on the exact cause of the deposition of the calcareous material. However, from our present knowledge, it appears that it is the local condition and not a general metabolic change which is the important factor determining the deposition of calcium salts in the unusual cases here recorded.

SUMMARY

Two unusual cases with calcareous deposits have been reported. In the first case, the deposits occurred in the epiphyses of most of the long bones. The patient lived only a few weeks, and had a peculiar deformity of the jaw and limitation of the movements of the other joints of the body. We were unable to find a report of any similar case in the literature.

The calcium deposits in the second case were in the skin and subcutaneous tissues. The underlying condition appeared to be either scleroderma or xeroderma pigmentosum.

Blood serum calcium and inorganic phosphorus determinations were made in both cases. The values found were 9.3 mg. and 9.7 mg. of calcium per hundred cubic centimeters; and 4.5 and 4.4 mg. of phosphorus. These determinations are essentially within the normal limits.

From the microscopic examination of the tissues and the determination of the blood serum calcium and inorganic phosphorus, it would appear that the local condition is the important factor which determined the deposition of the calcium salts in these cases.

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[8] Mosbacher, E.: Deutch. Arch. f. klin. Med. **128:** 107, 1918.

TREATMENT OF EARLY HEREDITARY SYPHILIS WITH INTRAMUSCULAR INJECTIONS OF SULPHARSPHENAMIN *

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The peculiar difficulties of administering any form of intravenous therapy to small infants are well known. The median longitudinal sinus has proved most valuable as a route for giving fluids intravenously, or for transfusion, but, occasionally, attempts to administer arsphenamin and neo-arsphenamin intrasinusly have been attended with fatal results. At times, the superficial veins of the scalp are prominent and may be utilized, but often the external jugulars are the only veins available, and at times even these are not visible. It is often difficult, except for those who have had much practice, to make a clean puncture into a jugular vein which is covered by skin, fascia, and platysma muscle. As a result, various attempts have been made to prepare arsenicals in a form suitable for subcutaneous, intramuscular and rectal administration. Neo-arsphenamin, specially neutralized for intramuscular injection, can now be obtained, but its use is attended by the frequent formation of indurated areas, and occasionally sloughs have occurred. It is not the purpose of this paper to discuss the relative merits of these different forms of antisyphilitic therapy, but to record the results obtained by intramuscular injections of sulpharsphenamin in the treatment of young infants suffering from hereditary syphilis. The sulpharsphenamin reported on is sulfarsénol (the French brand). We are now making tests with the American made drug in a series of cases and expect to publish the results shortly.

Sulpharsphenamin was first described in September, 1919, by Levy-Bing, Lehnhoff-Wyld and Gerbay.[1] In chemical structure, it is closely related to neo-arsphenamin, its molecular formula ($C_{12}H_{11}As_2N_2CH_2O\,SO_2Na$) differing from the latter only by the addition of a single oxygen atom. It is a pale yellow powder, having, in solution, an odor

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* Received for publication, Sept. 17, 1923.

* From the Harriet Lane Home, Johns Hopkins Hospital, and the Department of Pediatrics, Johns Hopkins University.

* This clinical trial of sulpharsphenamin was suggested by Dr. Carl Voegtlin of the United States Public Health Service, who furnished us with a supply of the drug for our studies.

1. Levy-Bing, Lehnhoff-Wyld, and Gerbay: Un nouveau composé arsenical: Le sulfarsénol, Ann. d. mal. ven. **14**:520 (Sept.) 1919.

faintly suggestive of carbon bisulphid. The above mentioned authors demonstrated that it was more stable than arsphenamin or neo-arsphenamin (there was practically no change in composition after standing twenty-four hours in test tubes exposed to the air); that it was from one-half to one-third as toxic for mice as neo-arsphenamin, and that it was more soluble than either arsphenamin or neo-arsphenamin. They obtained good results in a series of thirty-three adults, whom they treated for a short time.

Since this first publication, the drug has been given a rather wide clinical trial intravenously (Levy-Bing, Lehnhoff-Wyld and Gerbay;[1] Bernard,[2] Gallonnier[3]), subcutaneously (Emery and Morin;[4] Mendes Da Costa;[5] Yernaux and Bernard[6]), and intramuscularly (Galonnier;[3] Mendes Da Costa;[5] Chatellier;[7] Duroeux;[8] Levy-Bing and Gerbay[9]) by a number of European clinicians. Many of them are enthusiastic about their results. However, Papegaaij and Rinsema[10] did not consider sulpharsphenamin given subcutaneously as effective as neo-arsphenamin given intravenously, either in the rapidity of the disappearance of spirochetes from mucous lesions, or in the frequency with which a negative Wassermann reaction could be obtained. None of the clinical trials, so far, have dealt with infants.

Voegtlin, Johnson, and Dyer[11] have aroused new interest in this drug by their studies of the synthesis, and chemical and pharmacologic properties. This preparation is now being manufactured by several American firms.

DOSAGE

The arsenic content of neo-arsphenamin is 19 per cent., while that of sulpharsphenamin is 21 per cent. The dose of neo-arsphenamin usually given is 15 mg. per kilogram of body weight. Because of the approximate similarity in the content of arsenic, most clinicians have taken this figure as the maximum dose for sulpharsphenamin. One manufacturer of sulpharsphenamin states that when arsenic is well tolerated, the dose may be increased until 15 mg. per kilogram of body weight is given. Duroeux,[8] in treating adults, began with small doses (0.12 gm.), increasing the dosage up to 0.60 gm. In testing the human tolerance for the drug, Levy-Bing, Lehnhoff-Wyld and Gerbay [1] gave a dose as large as 0.9 gm. to an adult without provoking any reaction. In determining the toxic dose for mice, they found that the toxicity of sulpharsphenamin was from one half to one third that of neo-arsphenamin. Voegtlin, Johnson, and Dyer,[11] in working with sulpharsphenamin, demonstrated that the minimum lethal dose for albino rats was from 320 to 480 mg. per kilogram. The official U. S. regulations governing the sale of neo-arsphenamin required only that it pass a test of 200 mg. per kilogram. Experimental investigation of the power of the different arsenicals to penetrate the tissues has shown that the larger the dose the greater the penetration.[12] For this reason; in view of the lower toxicity, and because it is well known that babies usually will tolerate proportionately larger doses of active drugs than adults, it seemed to us that the dose might be increased. Accordingly, after observing that the smaller doses were well borne, we began to use larger amounts, and are now giving doses of 20 mg. per kilogram of body weight. We have given this dose many times, but have never seen a serious reaction.[13] This means that an infant receives 1.47 times as much arseńic as we previously would have given him in the form of neo-arsphenamin.

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[2] Bernard, R.: Le sulfarsénol, Scapel **19**, October, 1919.

[3] Galonnier, P.: Recherches sur l'administration et l'elimination de sulfarsénol au cours de la syphilis, Toulouse, 1920.

[4] Emery and Morin, A.: Traitement de la syphilis par les injections sous-cutanees d'arsénobenzènes, Bull. méd. **34**:549 (June) 1920.

[5] Mendes Da Costa, S.: Sulfarsénol als antisyphiliticum, Nederl. Tijdschr. v. Geneesk. **2**:513 (Aug. 7) 1920.

[6] Yernaux and Bernard: Contribution au traitement de la syphilis par le sulfarsénol, Scapel **24**:593 (Dec.) 1919.

[7] Chatellier, L.: Le traitement de la syphilis et de quelques dermatoses par le sulfarsénol intramusculaire, Toulouse méd. **5**:176 (March) 1920.

[8] Duroeux, L.: De l'influence du sulfarsénol sur la réaction de Bordet-Wassermann dans le traitement de la syphilis, Progrès méd. **36**:155 (April 9) 1921.

[9] Levy-Bing and Gerbay: Essai d'une therapeutique arsenicale intramusculaire, Ann. d. mal. ven. **15**:15 (Jan.) 1920.

[10] Papegaaij, J., and Rinsema, P. G.: Mededeelingen over Sulfarsénol, Nederl. Tijdschr. v. Geneesk. **2**:560 (July 30) 1921.

[11] Voegtlin, C.; Johnson, J. M., and Dyer, H.: Sulpharsphenamine: Its Manufacture and Chemotherapeutic Properties, Pub. Health Rep. **37**:2783-2798 (Nov. 10) 1922.

The twenty-one cases on whom our report is based were seen in the course of routine examinations in the Harriet Lane Home and Dispensary. All of the patients were less than 1 year of age, and presented the clinical picture of early hereditary syphilis. The diagnosis in all but one case was confirmed by Wassermann tests of the blood. In one patient, in whom the suspicion of syphilis was strong because of a positive Wassermann reaction in the mother and the presence of snuffles, treatment with arsenic was delayed until the age of 3 months, when his Wassermann reaction had become positive. In the interim, treatment with mercury by inunctions was administered. In a number of the patients, diagnosis was aided by the characteristic roentgenographic picture of the extremities. So far as possible, a record was kept of the individual lesions—snuffles, skin rashes, condylomas, rhagades, pseudoparalyses, etc.—and their duration after the beginning of treatment was noted. The Wassermann test was not made after each treatment but usually only at the beginning of each new course.

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[12] Voegtlin, C.; Smith, H. W.; Dyer, H., and Thompson, J. W.: Penetration of Arsenic into the Cerebrospinal Fluid, etc., Pub. Health Rep. **38**:1003-1013 (May 11) 1923.

[13] In a number of cases the dose was increased to 22 or 23 mg. per kilogram. In all but one case, this dose was tolerated. In this case, the injection was followed by a rather severe gastro-intestinal disturbance. As the incident occurred in the month of July, when such disturbances are relatively common in otherwise normal infants, we did not feel certain that it was a result of the arsenical treatment.

METHOD

Treatments were given at weekly intervals until a course of six injections had been completed. The patients were then allowed a rest period of two months before a second course was commenced. During the rest period, mercury inunctions were given. A portion of one-third strength blue ointment (diluted mercurial ointment, U. S. P.) about the size of a pea was applied each morning on a flannel abdominal binder. The exertions of the infant (crying, kicking, etc.) furnished the friction necessary for absorption. Our plan of treatment is to give three complete courses of sulpharsphenamin after a negative Wassermann reaction has been obtained. Four complete courses will be, then, the minimum number that any child will receive.

At the time of this publication, all of our twenty-one patients have completed one course; seven, two courses, and four, three courses.

Sulpharsphenamin has been given by others, intravenously, subcutaneously and intramuscularly. We have used the intramuscular route entirely, most of the injections being made into the muscles of the buttocks. It has seemed to us that fewer local reactions were obtained when precautions were taken to insure that all of the solution went into the muscles and none into the subcutaneous tissue. A sharply pointed needle of fine bore (No. 22) is used with a 2-c.c. Luer syringe. The solution to be injected is usually less than 1 c.c. in volume. This is drawn into the syringe, and then the rest of the syringe is filled with air. The site selected for the injection is cleaned with iodin and alcohol and the needle is wiped with dry sterile gauze. With the syringe held in a perpendicular position, the needle is plunged directly into the muscle tissue. The injection can then be made so that the solution enters the muscle first, and the last drops can be ejected from the needle by forcing the air in the syringe into the muscle. The needle is withdrawn slowly to allow the tissues time to contract and prevent return of the solution along the needle tract.

COMMENT

It is generally agreed that there are fewer and less intense local reactions from the preparation when concentrated solutions occupying a small volume are used. We have been obtaining the drug in ampules containing 0.6 gm. The contents of one of these is dissolved in 2.7 c.c. of sterile, freshly distilled water. The total volume will then be 3.0 c.c., a 20 per cent. solution. The maximum dose is reached when the baby is given 0.1 c.c. of this solution per kilogram of weight.

General reactions following the intramuscular injection of sulpharsphenamin are not common, and when present are mild. We have on several occasions noted slight gastro-intestinal disturbances (vomiting and increase in the number of stools) of about twenty-four hour's duration. These reactions have never been so severe or so frequent as those following the intravenous injection of neo-arsphenamin. Doble,[14] in contrast to the experience of the French investigators, found that, in a few of his patients, a Herxheimer reaction, which was very slight and transitory, occurred. With one of our patients (J. P.), a white male infant, 2 months of age, who had been having convulsions, and who had spinal fluid pleocytosis, the number of cells in the spinal fluid increased after his first and second treatments. However, there was no noticeable constitutional reaction, and the infant gained 15 ounces (425 gm.) during the period. After the third treatment, the convulsions ceased.

Levy-Bing and Gerbay [9] found that in the majority of their patients there was no local reaction. Some of them complained of a sensation of heaviness and muscular stiffness, which rarely lasted more than from twenty-four to forty-eight hours. Emery and Morin [4] had a similar experience. Papegaaij and Rinsema,[10] who had given about 1,100 intramuscular injections in the buttocks, found that there was acute pain of short duration following all injections; that induration at the site of injection was uncommon, and that abscesses never occurred. Our experience with infants is somewhat similar. Pain is more difficult to recognize in an infant than in an adult. However, we have not received complaints from the mothers of dispensary patients, nor have the babies under our own observation in the hospital, exhibited signs of pain, except at the time of the injection. Up to the present time, we have made 349 injections. In twenty-four instances, or 7.7 per cent. of the cases, an indurated area from 1 to 2 cm. in diameter developed by the following week. There was never any evidence that these "lumps" were tender or painful, but they disappeared rather slowly (in from one to three months). We have never seen an abscess or a slough develop following the intramuscular injection of sulpharsphenamin.

In our series, there were four babies who had the characteristic maculopapular eruption of congenital syphilis. In one of these, the eruption disappeared seventeen days after the beginning of treatment.

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[14] Doble, F. C.: Sulfarsénol in the Treatment of Syphilis, Lancet **2**:243, 1920.

In the other three patients, it was absent one week after the second injection had been given. In all four of these patients, improvement commenced two or three days after the first treatment. The rash appeared less elevated and the color had begun to fade. There were four colored infants who had circinate syphilids of the face and extremities. In all of these, the skin was practically clear when they were brought back for the second treatment, except for slight pigmentation, which rapidly became less evident after subsequent treatments.

Two infants had anal condylomas. Improvement was noticed during the first week, but healing was not complete until the end of the third week in one patient and the fourth week in the other. Rhagades and fissures of the lips were present in two patients. In one of these, healing occurred after two treatments; in the other, only after the completion of a course of six treatments.

Difficult and noisy respiration due to swelling and discharge from the nasal mucous membranes ("snuffles") is one of the most constant findings in early hereditary syphilis. This symptom was present in sixteen of our twenty-one patients. In only one of the infants was the nasal discharge bloody. The administration of arsenic nearly always results in improvement in this symptom, but since there is actual hypertrophy of the mucous membranes, and at times underlying periostitis, its final disappearance must be slow. After the first course of treatments, the "snuffles" had entirely disappeared in four patients, and was improved in nine and unchanged in one. In the two remaining cases, the notes on the duration of the symptom were not complete.

There were five infants who had pseudoparalysis. In each of these patients, pain, tenderness and swelling had subsided markedly when they were brought back for the second treatment. In one of them, the movements were entirely normal after the first treatment. Three required two treatments and one three treatments before the symptom completely disappeared. In each of these patients, the nature of the lesion was confirmed by the characteristic roentgenographic picture.

Our notes in regard to the decrease in size of enlarged spleens and epitrochlear glands are not sufficiently complete to enable us to draw any conclusions regarding the result of treatment.

Despite the limitations of a purely laboratory method of diagnosis, the Wassermann test is and probably will remain the most important aid in the diagnosis of syphilis and in determining the effect of treatment. Duroeux,[8] in a series of 162 adults treated with weekly injections of sulpharsphenamin, noted that the Wassermann reaction became negative in 68 per cent. after one course (ten injections), in 19 per cent. after two courses, and in the remaining 13 per cent. after three courses. He was able to obtain even better results by giving the injections at more frequent intervals. The Wassermann tests in our series were made by the syphilis department of the Johns Hopkins Hospital according to the technic described by Keidel and Moore.[15] Of the twenty patients whose Wassermann reaction of the blood were positive, eleven, or 55 per cent., gave negative reactions after the completion of one course. Since, in most instances, the second Wassermann test was not made until the beginning of the next course of treatments, this means that the reaction had become negative and remained so over a period of two months without arsenic treatment. In one patient, a negative reaction was obtained one week after the first injection, and this negative reaction was permanent. One patient with a positive reaction after one course gave a negative reaction after two courses. In the one patient whose reaction remained positive after two courses, very small doses had been used. After a third course, in which the size of the dose was increased, the reaction became negative.

Throughout the period of treatment, it was repeatedly noted that the general condition of the patients was markedly improved; that they seemed less susceptible to infections, gained in weight, and gradually regained the appearance of normal infants.

Two illustrative case histories are given:

REPORT OF CASES

CASE 1.—*History.*—W. B., boy, white, aged 5 weeks, admitted to Harriet Lane Home, Oct. 31, 1922, with a diagnosis of early hereditary syphilis, gave the following history: The father, aged 27 years, had been treated for syphilis, and the mother, aged 29 years, had a positive Wassermann reaction. The patient was the second child. The first was born prematurely (at eight months) and died in two days. The birth of the patient was normal. The present complaint was: (1) eruption over the skin, of five days' duration, and (2) snuffles, of three weeks' duration.

Physical Examination.—The patient was fairly well developed and well nourished. There was a red, slightly elevated, maculopapular eruption over the face, with some incrustation and a marked fissuring of the lips, extending into surrounding skin for one quarter inch (0.6 cm.). Over the extremities, there was an eruption of the same nature, which was symmetrically distributed. There were many maculopapular lesions varying, in size from one-quarter to three-eighths of an inch (0.6 to 0.9 cm.) in diameter. Many of these were confluent. There was a slight scaling on the wrists and some desquamation on the palms. The inguinal glands were palpable; the epitrochlears were not enlarged. There was a yellowish discharge from each nostril. No distension or rigidity of the abdomen was noted. There was a slight umbilical hernia. The spleen was 2 cm. below the left costal margin. The remainder of physical examination was negative.

Laboratory Examination.—The white blood count was 7,500; the urine was negative. Culture of the nasal discharge was negative for *B. diphtheriae.* The blood Wassermann reaction was positive. A roentgenogram of the extremities revealed evidences of syphilitic osteochondritis (Fig. 1).

Treatment.—Administration of sulpharsphenamin was begun, Nov. 7, 1922, in the routine manner, except that two treatments each week were given in the first course until eight treatments had been given. Following the first injection, the eruption faded rapidly and by the seventeenth day (Nov. 24), after four injections, it had entirely disappeared (Fig. 2).

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[15] Keidel, A., and Moore, J. E.: Wassermann Reaction in the Johns Hopkins Hospital, Bull. Johns Hopkins Hosp. **34**:16 (Jan.) 1923.

This course of treatment was completed, December 5, and the patient was discharged for six weeks. The mother was instructed to apply diluted mercurial ointment by means of an abdominal binder daily. The patient had improved greatly and was discharged weighing 10 pounds and 13½ ounces (4,832.6 gm.). Jan. 30, 1923, the blood Wassermann reaction was negative.

The second course, six treatments, was started, January 30. There was no reaction, either local or general, to any of the injections. The patient now, except for slight scars from old rhagades and a palpable spleen, showed no signs of hereditary syphilis. The Wassermann reaction was negative; he was gaining in weight, and was normal in appearance for his age. May 15, the blood Wassermann reaction was negative.

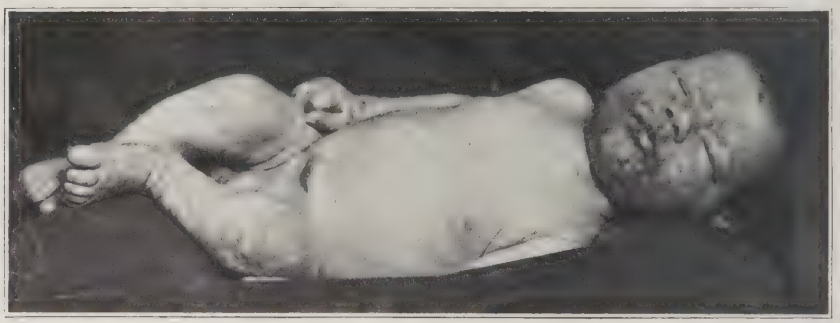

Fig. 1 (Case 1).—Appearance of patient before treatment was commenced, showing maculopapular eruption.

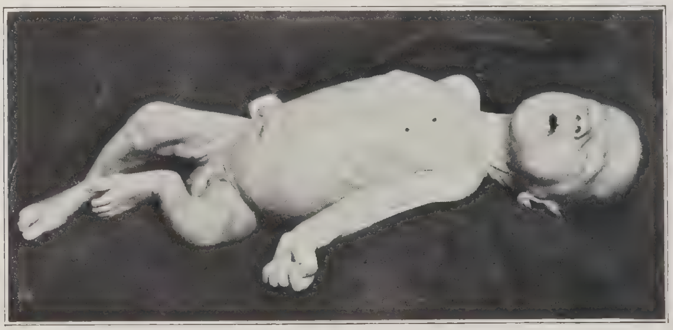

Fig. 2 (Case 1).—Appearance of patient after seventeen days' treatment (four injections), showing condition of skin.

The third series, six treatments, was started, May 8. There was only one slight local reaction from treatment, in form of a lump in the buttocks. The patient has now received three courses of treatments. The Wassermann reaction has been negative since the first course. There are no signs of hereditary syphilis except the scars about the lips and a palpable spleen. The patient is 9 months old, weighs 20 pounds and 12 ounces (9.43 kg.) and in appearance is a normal healthy child.

Case 2.—*History and Examination.*—E. B., girl, colored, aged 6 weeks, admitted to Harriet Lane Dispensary, May 5, 1923, with a diagnosis of early hereditary syphilis, on admission had a definite pseudoparalysis of both upper extremities, and cried when she was handled. There was a maculopapular eruption on the extremities and macular lesions on the palms and soles. The epitrochlears and the spleen were palpable. The blood Wassermann reaction was positive. A roentgen-ray examination of the extremities revealed evidences of syphilitic osteochondritis.

Treatment.—One course of six weekly injections of sulpharsphenamin was given. The only reaction was a small lump in the right buttock after one injection. After the second treatment, the eruption disappeared, and the movements of the upper extremities were normal. The Wassermann reaction was negative two months after one course of treatment.

CONCLUSIONS

1. Sulpharsphenamin is a safe and easily administered arsenical preparation for the treatment of hereditary syphilis in infants.

2. Sulpharsphenamin can be safely given to infants in a dose as large as 20 mg. per kilogram of body weight.

3. The reactions, either general or local, to treatment are very slight.

4. In 55 per cent. of the patients, the Wassermann reaction became negative after one course of six treatments.

5. The symptoms of hereditary syphilis rapidly disappear, and the patient's general condition quickly improves after treatment.

6. Because of the ease with which sulpharsphenamin can be administered, it should be very useful to the practitioner who is not adept at intravenous therapy.

SUMMARY OF TWENTY-ONE CASES

C. R.—Snuffles, slight improvement after 1 course of treatment; circinate syphilid, disappeared after 2 treatments; palpable spleen, remained palpable after 1 course of treatment; positive blood Wassermann reaction, negative after 1 course of treatment.

M. W.—Snuffles, slight improvement after 1 course of treatment; enlarged spleen, no change after 1 course of treatment; epitrochlears enlarged, no change after 1 course of treatment; anal condylomas, improved rapidly and were healed 1 week after 4th weekly injection; positive blood Wassermann, negative after 1 course of treatment.

B. R.—Enlarged spleen, no change after 1 course of treatment; enlarged epitrochlears, no change after 1 course of treatment; anal condylomas, completely healed after 3 treatments; positive blood Wassermann reaction, remained positive after 1 course of treatment.

L. H.—Snuffles, no note made; cracked lips, and rhagades, sores on lips healed rapidly after 2d treatment; macular syphilid, completely healed after 2 treatments; enlarged spleen, no change; negative blood Wassermann reaction, remained consistently negative during 2 courses of treatment.

E. C.—Pseudoparalysis, right arm, child moved arm normally after 2 treatments; positive blood Wassermann reaction, was positive after 1 course, doubtful positive after 2 courses of treatment and negative after 3 courses.

C. B.—Bloody nasal discharge, improved after 1 course of treatment; circinate syphilid, disappeared after 2 treatments; enlarged spleen, no change after 1 course of treatment; enlarged epitrochlears, no note made; positive blood Wassermann reaction, negative after 1 course of treatment.

A. H.—Snuffles, disappeared after 4 treatments; pseudoparalysis of both legs, moved normally after 1 treatment; enlarged epitrochlears, no change after 1 course of treatment; positive blood Wassermann reaction, remained positive after 1 course of treatment.

E. B.—Snuffles, markedly improved after 4 treatments; maculopapular syphilid, disappeared after 2 treatments; pseudoparalysis (arms), movements of arms normal after 3 treatments; enlarged spleen, no improvement after 1 course of treatment; positive blood Wassermann reaction, negative after 1 course of treatment.

H. H.—Snuffles, disappeared after 4 treatments; enlarged spleen, no note made; positive blood Wassermann reaction, negative after 1 course of treatment.

J. McK.—Snuffles, improved after 1 course of treatment; positive blood Wassermann reaction, remained positive after 1 course of treatment.

L. F.—Positive blood Wassermann reaction, remained positive after 1 course of treatment.

W. B.—Snuffles, greatly improved after 1 course of 8 treatments; maculopapular syphilid, had disappeared by 17th day after treatment was stared; rhagades and cracked lips, healed by end of 6th treatment; enlarged spleen, no note made; positive blood Wassermann reaction, negative after 1st course of 8 treatments and has remained negative for 7 months with 2 consecutive courses of 6 treatments each.

J. B.—Snuffles, disappeared after 1st course of treatment; pseudoparalysis (both legs), movements normal after 1 treatment; positive blood Wassermann reaction, negative after 1 course of treatment and has remained so for 7 months with 2 consecutive courses of treatment.

J. C.—Positive blood Wassermann reaction, negative after 1 course of 4 treatments, and has remained so for 4 months with 1 subsequent course of treatment.

R. P.—Snuffles, greatly improved after 3 treatments; pseudoparalysis, upper and lower extremities, movements normal after 2 treatments; positive blood Wassermann reaction, remained positive after 4 treatments.

I. G.—Snuffles, greatly improved after 1 course of treatment; positive blood Wassermann reaction, negative after a single injection.

O. P.—Snuffles, no improvement after 1 course of treatment; positive blood Wassermann reaction, negative after 1 course of treatment.

I. F.—Snuffles, no note made; maculopapular syphilid, healed by end of 2nd treatment; palpable spleen, no improvement after 1 course of treatment; positive blood Wassermann reaction, remained positive after 1 course of treatment.

J. S.—Circinate syphilid, only slight pigmentation of skin remained after 2 treatments; positive blood Wassermann reaction, remained positive after one course of treatment; negative after two courses.

E. W.—Snuffles, improved rapidly as soon as treatment was begun and had almost entirely disappeared by end of 1st course of treatment; rhagades, greatly improved and had healed by end of 1st course of treatment; positive blood Wassermann reaction, negative after 1st course of treatment and has remained negative for 5 months with one subsequent course of treatment.

H. W.—Snuffles, slight improvement after 1 course of treatment; positive blood Wassermann reaction, Wassermann was "suggestive negative" after 2 treatments and negative after 5 treatments.

VITAL CAPACITY AS AN AID IN DIAGNOSIS OF TRACHEOBRONCHIAL ADENOPATHY IN CHILDREN FROM FIVE TO TWELVE YEARS OF AGE

ITS SIGNIFICANCE IN EVALUATION OF VITAL CAPACITY MEASUREMENT OF AVERAGE NORMAL CHILDREN *

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In a previous paper on the measurement of vital capacity of children, we indicated that the low values obtained by this test in some of our apparently normal subjects was probably due to tracheobronchial adenopathy.[1] The evidence in support of this view was obtained from the roentgenologic findings, in all those instances studied by this method at the time that the work was prepared for publication. The interpretation of a relationship existing between the vital capacity of the lungs and tracheobronchial adenopathy is one of considerable importance, since it implies (1) that the measurement of the vital capacity can be used as a valuable adjunct in the diagnosis of tracheobronchial adenopathy and (2) that, in the attempt to establish a standard of vital capacity for the average normal child, the incidence of this disease would materially modify the result.

At the outset, it is essential to summarize the present conception of the diagnosis, incidence and clinical significance of tracheobronchial adenopathy in children from 5 to 12 years of age, as indicated by a survey of the recent literature.

The diagnosis is considered one of great difficulty, as the physical signs are indefinite. D'Espine's sign is most generally used.[2] Its value, however, is considered uncertain, because of the discrepancy in the findings and interpretations of various investigators.[3] The roentgenray interpretation of hilum, root and trunk shadows is also attended by

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* Received for publication, Sept. 17, 1923.

* From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

[1] Wilson, May, and Edwards, D. J.: Standards for Normal Vital Capacity for Children; the Lung Capacity in Certain Intrathoracic Conditions, Am. J. Dis. Child. **22**:443-454 (Nov.) 1921.

[2] Much, H.: Tuberculosis of Children (translated by Dr. Marx Rothschild), New York, MacMillan Company, 1921, p. 93.

[3] Griffith, J. P. C.: Diseases of Infants and Children, Vol. 2, Philadelphia, W. B. Saunders Co., 1919, p. 556.

some uncertainty, differences in opinion being due to the variation in technic as well as to the fact that the norm for children is difficult to standardize.[4] There seems to be a general agreement that an increase in the hilum shadow is indicative of engorgement and enlargement of the intrathoracic glands, and that the accompanying extensive linear markings radiating to the lung periphery, particularly the upper parts of the lung, may be considered pathologic.[5]

As to the clinical significance of tracheobronchial adenopathy, two important facts are stressed:[6] 1. Engorgement of the intrathoracic glands accompanies and is a sequel of most infections, particularly those involving the respiratory tract, such as measles and pertussis. 2. The seat of tuberculous infection, both latent and active in children, is in the intrathoracic glands.[7] These considerations suggest that the incidence of tracheobronchial adenopathy in any group of children is likely to be high, and that the degree and permanency of the involvement will vary with the etiologic factor.

Although realizing the difficulties of any comparative study based on still uncertain criteria, as is evident from the summary of the diagnosis as outlined above, we purpose in this investigation to make a comparative study of (1) the vital capacity and roentgen-ray findings of an arbitrarily selected group of average children, apparently normal and ranging in age from 5 to 12 years, and (2) the vital capacity and roentgen-ray findings of a selected group of children with tracheobronchial adenopathy.

The subjects selected for comparative roentgenographic study and vital capacity measurement may be considered under two general groups. The first group comprises eighty-three subjects, arbitrarily selected from a total of 360 apparently normal children (who were observed in the investigation for the normal standards of vital capacity[1]). All of these children passed a routine physical examination. They were apparently healthy, and were attending public or private school in New York City. We shall subdivide this group into two divisions, one made up of fifty average white children selected without regard to race, and the other thirty-three colored children. The other main group of subjects considered in this study were selected because of predisposing history, clinical symptoms, physical signs or roentgen-ray evidence justifying the clinical diagnosis of tracheobronchial adenopathy.

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[4] Pottenger, F. M.: Clinical Tuberculosis, St. Louis, C. V. Mosby Company, 1922, p. 114.

[5] Dunham, Kennon: Stereoroentgenographic Studies of Pulmonary Tuberculosis, Troy, N. Y., Southard Company, 1915, p. 522.

[6] Fleischner, E. C.: Bronchial Lymphadenopathy, Nontuberculous, J. A. M. A. **79**:175 (July 15) 1922.

[7] Fishberg, Maurice: Pulmonary Tuberculosis, Ed. 2, Philadelphia, Lea and Febiger, 1919, p. 395.

METHOD AND TECHNIC

The vital capacity measurement was determined as described in the preliminary investigations.[1] All known factors which tend to diminish the vital capacity measurement were considered, and all subjects giving evidence of such complicating factors were eliminated from this study.

A graph of the vital capacity readings of 360 average, apparently normal children, is included for comparative study (Fig. 7).

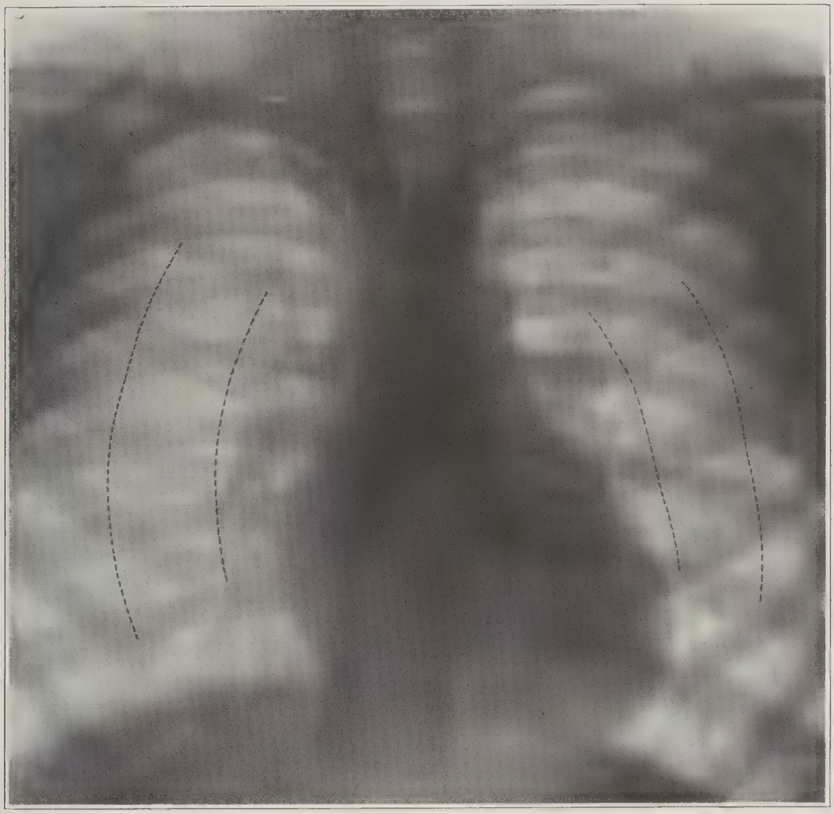

Fig. 1.—Normal subject with a grading of 1 +.

The roentgenologic examinations, with films, were supplemented by confirmatory fluoroscopic and stereoscopic examinations in the majority of cases. The roentgen-ray technic used, in the main, was that described by Dunham and Blackfan.[8] In a small number of cases, serial films were taken over a period of a year or more. The degree and the extent of the hilum shadow and the pulmonary markings were arbitrarily graded; those indicating little evidence of increase in the hilum shadow with lung parenchyma fairly free and clear (Fig. 1) as 1 +; those showing definite increase in the hilum shadow with pulmonary markings extending midway to the lung periphery (Fig. 2) as 2 +, and those revealing extensive increase in the hilum shadow with linear markings pronounced and extensive radiating to apices and lung periphery (Fig. 3) as 3 +.[9]

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[8] Dunham, H. K., and Blackfan, Kenneth: Preliminary Report on Clinical and X-Ray Findings in the Chests of Normal Children, Tr. Nat. Tuberculosis Ass'n, 1921.

Since the completion of this investigation, there has been published by the National Tuberculosis Association, a report containing an excellent composite diagrammatic roentgenogram of the normal chest of the child, showing a division of the lung into three vertical zones, for "convenience of description" (Fig. 5). The arbitrary divisions which we have made in our preliminary and present reports, i. e., the gradations of 1 +, 2 + and 3 +, are comparable to the division of Zone I, Zone II, and Zone III, respectively, shown in their illustration.

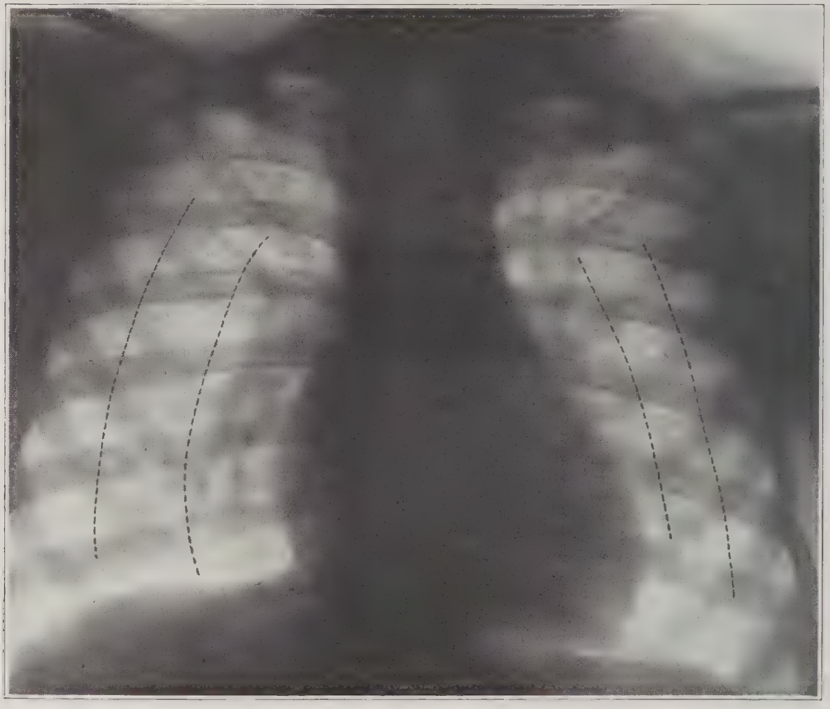

Fig. 2.—Normal subject with a grading of 2+.

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[9] These notations were made without the knowledge of vital capacity readings, and were checked three different times by us. Likewise, many of the films were seen, and our interpretations corroborated by disinterested, competent observers.

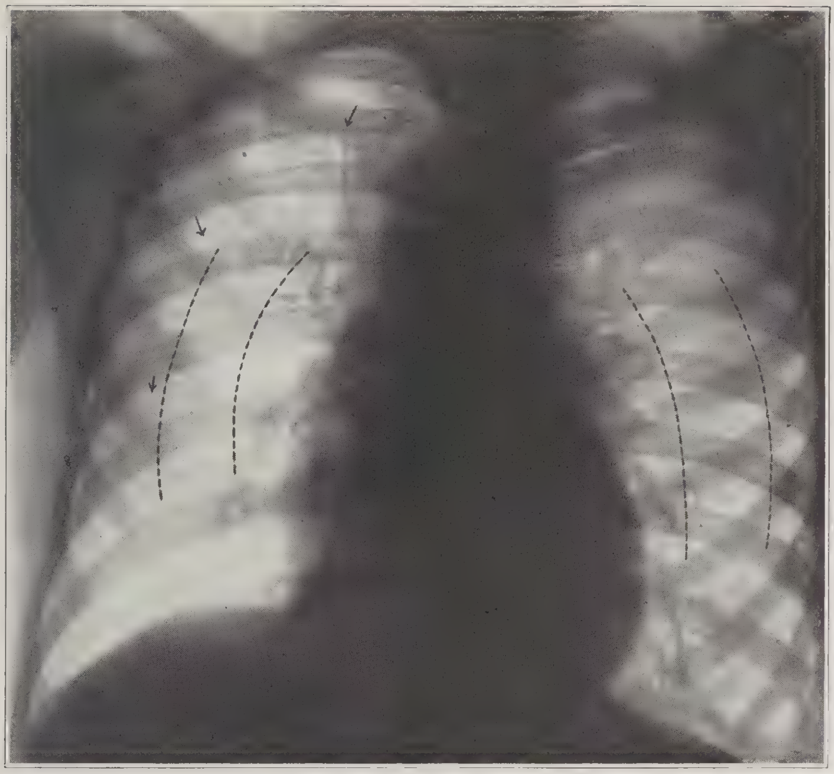

Fig. 3.—Normal subject with a grading of 3 +.

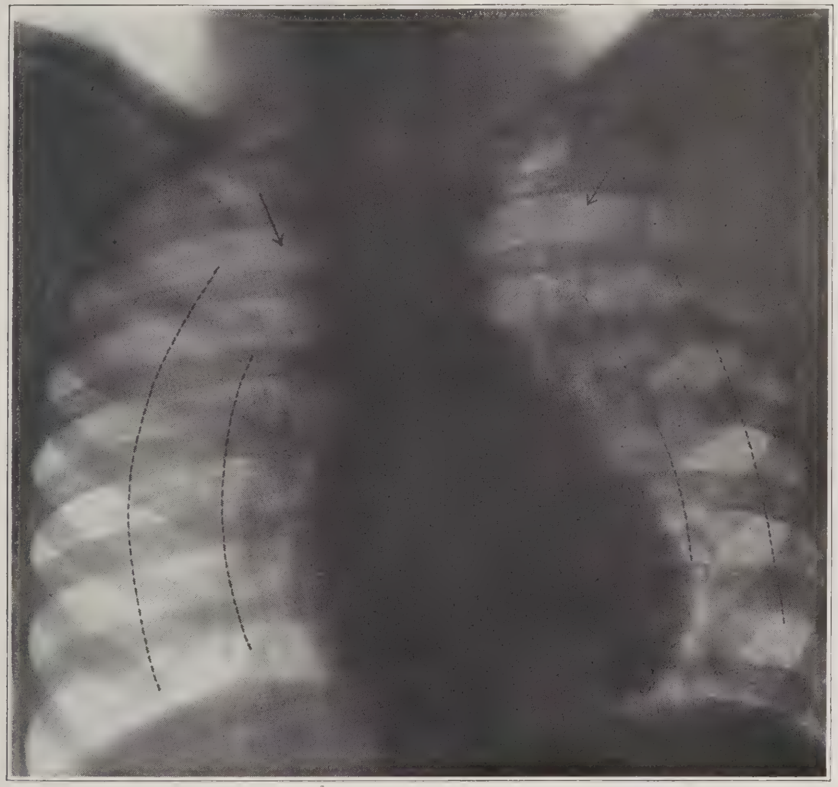

Fig. 4.—Chest of subject with tracheobronchial tuberculosis.

RESULTS

A comparative analysis of the roentgen-ray findings and vital capacity values observed for the normal group, as shown by Table 1, A and B, indicates that 16 per cent. of the white subjects and 84 per cent. of the colored subjects, with roentgen-ray findings graded as 3 +, showed average reductions in the vital capacity of 17 and 22 per cent., respectively, for each group. The remaining normal subjects, with findings graded as 2 + and 1 +, had vital capacity values within the average normal range, with slightly higher values for the 1 + group.

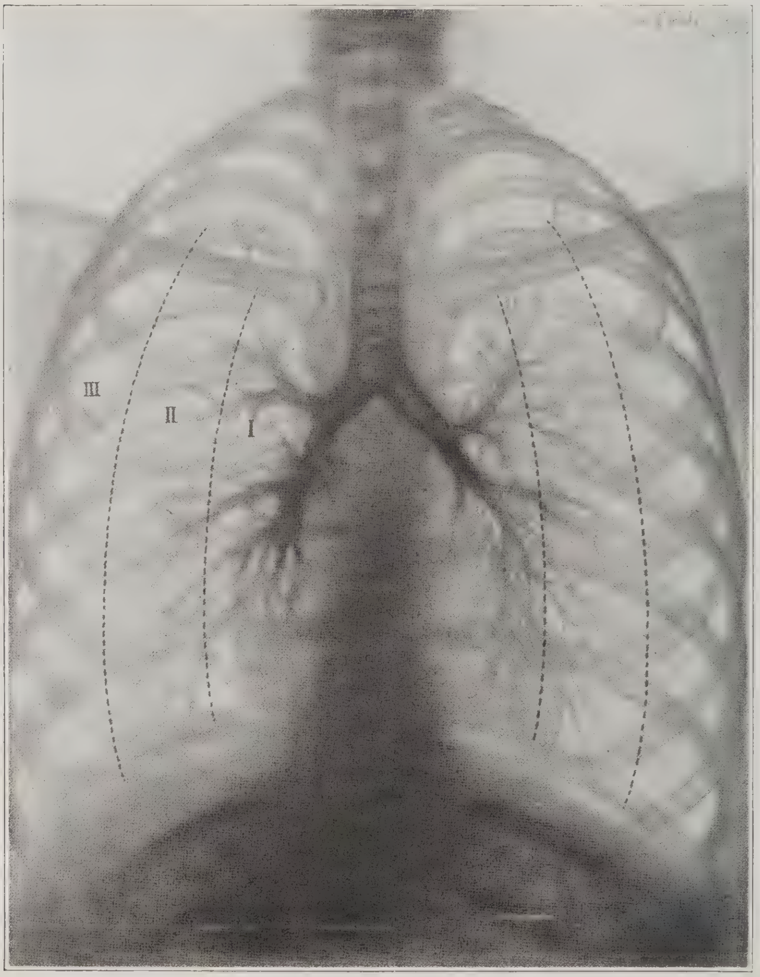

Fig. 5.—Composite diagrammatic roentgenogram of the normal chest of the child, showing the three zones (reproduced by courtesy of the American Review of Tuberculosis).

TABLE 1.—*Vital Capacity Readings and Roentgen-Ray Findings of Normal Subjects from 5 to 12 Years of Age*

	Roentgen Ray Graded 1+; Vital Capacity, Liters per Square Meters of Surface Area	Roentgen Ray Graded 2+; Vital Capacity, Liters per Square Meters of Surface Area	Roentgen Ray Graded 3+; Vital Capacity, Liters per Square Meters of Surface Area
A—White Subjects:			
	1.74 2.00	1.57 1.85 1.93	1.52
	1.85 2.04	1.72 1.81 1.92	1.52
	1.80 2.00	1.76 1.85 2.08	1.68
	1.81 2.15	1.72 1.80 2.00	1.66
	1.86 2.16	1.77 1.81 2.23	1.64
	1.81 2.19	1.75 1.81 2.28	1.65
	1.97 2.20	1.76 1.90 2.31	1.70
	1.90 2.20	1.75 1.97 2.45	1.60
	2.07	Average, 1.91	Average, 1.62
	Average, 1.98		(a reduction of 17%)
B—Colored Subjects:			
	1.80	1.77	1.36 1.47 1.61
	2.04	1.74	1.33 1.46 1.66
	Average, 1.92	1.74	1.38 1.46 1.66
		1.85	1.48 1.43 1.65
		2.09	1.42 1.55 1.68
		Average, 1.83	1.40 1.51 1.60
			1.47 1.54 1.66
			1.40 1.51 1.74
			1.48 1.51
			Average, 1.51
			(a reduction of 23%)

TABLE 2.—*Roentgen-Ray Findings and Vital Capacity Readings of Thirty Subjects from 5 to 12 Years of Age, with Tracheobronchial Adenopathy*

Type of Case	Vital Capacity, Liters	Roentgen-Ray Findings
Tuberculous:		
Active	1.12 (—42%)	All graded 3+
	1.35 (—[illegible]%)	
	1.42	
	1.47	
	1.42	
	1.43	
Latent	1.58 (—18%)	
	1.50	
	1.54	
	1.64	
	1.70	
Nontuberculous:		
Recent infection	1.41 (—28%)	
	1.43	
	1.48	
	1.44	
	1.44	
	1.53	
	1.59	
	1.58	
	1.60	
	1.74	
Asthma group	1.42	
	1.46	
	1.47	
	1.45	
	1.33	
	1.50	
	1.65	
	1.54	Graded 2+
	1.80	Graded 2+

The individual vital capacity values are, in the main, consistent with the average values obtained. These observations are in accord with those found in the preliminary investigation.

The result of the comparative analysis of the vital capacity readings and roentgen-ray findings in our second group of subjects (those with tracheobronchial adenopathy) is shown in Table 2. The roentgen-ray findings in all but two of the subjects of the asthma group are graded 3 +, confirming the clinical diagnosis. An average reduction of vital capacity of 23 per cent. was obtained for the group. There were greater individual reductions noted, particularly in subjects with symptoms of active infection, as much as 42 per cent. in one instance. These results show a close correlation between the vital capacity, roentgen-ray findings and clinical diagnosis.

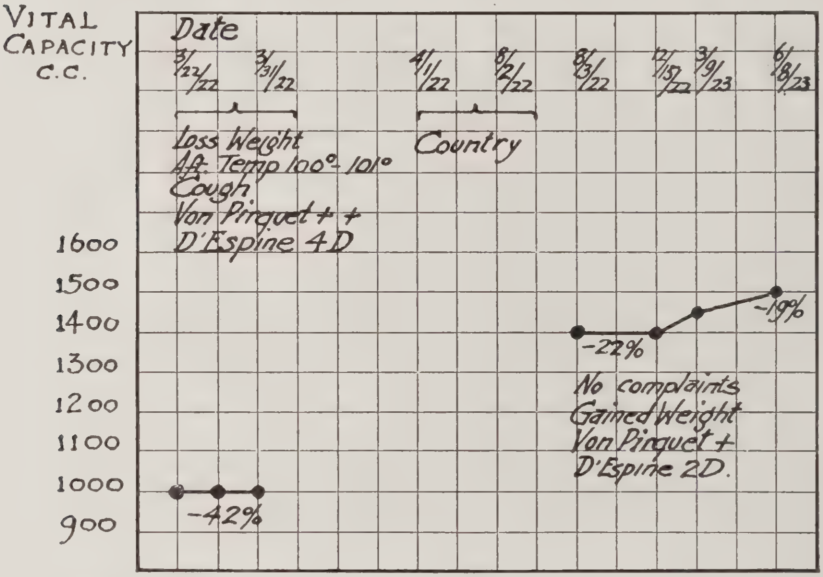

Fig. 6.—Record of vital capacity of girl (J. I., colored), 8 years of age, with tracheobronchial tuberculosis.

Some of the group with tracheobronchial adenopathy have been observed for a period of one or two years. The record of subject J. I. with tracheobronchial tuberculosis (Fig. 6) is of interest. It shows a reduction of vital capacity of 42 per cent. during the stage of active clinical symptoms. At periods of six months and one year later, when the condition was quiescent, the vital capacity still showed a reduction of 22 and 19 per cent., respectively. During the latter period, the child was apparently well and was attending school. Certain subjects with nontuberculous tracheobronchial adenopathy seemed to show a more rapid increase in the vital capacity than tuberculous subjects, a few coming within normal limits within from three to six months.

A comparative analysis of the plotted curves of combined vital capacity readings for subjects graded as 1 +, 2 + and 3 +, and the curve of vital capacity readings of 360 average normal children (Fig. 6) is of interest. It shows rather strikingly that subjects with a grading of 1 + and 2+, respectively, fall within the normal range, 1.74 and 2.14 liters per square meter of body surface, while subjects with a grading of 3 + cover the lower range of the normal curve, from 1.30 to 1.69 liters per unit of body surface.

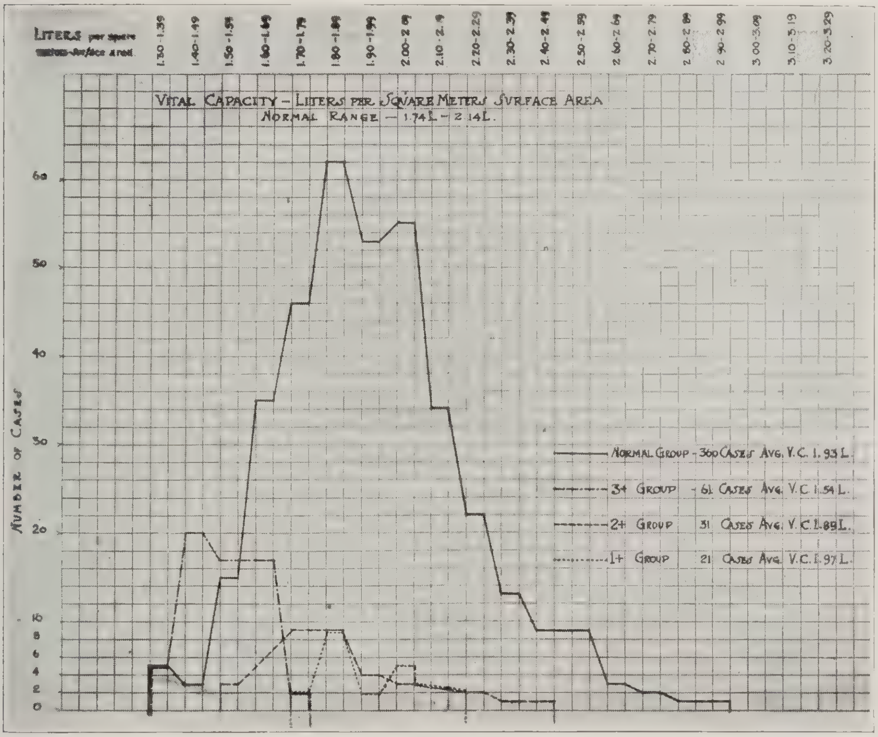

Fig. 7.—Comparative vital capacity curves of 360 average normal subjects, and subjects with tracheobronchial adenopathy.

COMMENT

We have attempted to contrast the vital capacity readings and the roentgen-ray findings obtained from a study of average children, apparently normal, with similar observations on subjects with clinical symptoms or physical signs of tracheobronchial adenopathy. We will first consider the results of our observations on normal subjects.

The most significant feature of these results is the roentgen-ray findings observed in 16 per cent. of normal white subjects and in 84 per cent. of colored subjects. The roentgen-ray findings described in these apparently normal children, which we have graded as 3 +, may be considered as pathologic. An explanation of the failure to eliminate these subjects from the normal group by anamnesis and physical examination may be found in the unreliability of a history, and the recognized difficulty of eliciting diagnostic physical signs of tracheobronchial adenopathy, as well as the frequent absence of these signs. Of clinical significance is the reduction of vital capacity obtained for the subjects graded as 3 +, averaging 17 per cent. for the white subjects and 23 per cent. for the colored subjects. These findings indicate that, among a group of apparently normal children, one may expect to find a certain percentage of subjects who will show a diminished vital capacity, and will give accompanying roentgenologic evidence of tracheobronchial adenopathy. This would seem to be particularly true of colored subjects, possibly because of their susceptibility to such infections as tuberculosis.

A further consideration of the roentgen-ray findings in normal subjects giving vital capacity readings within normal limits lends additional support to the conclusion that the shadows observed, and graded as 1 + and 2 +, respectively, are to be interpreted as within the normal range. This view coincides with the findings reported by the National Tuberculosis Association, previously referred to.

Of clinical significance is the close relation between the roentgen-ray findings and the vital capacity readings of these subjects. This is well brought out by a comparison of the superimposed curves of combined vital capacity readings (Fig. 7). They show that subjects with a grading of 3 + cover the lower range of the normal curve, indicating that these individual low vital capacity readings may be due to tracheobronchial adenopathy. The fact that subjects with a grading of 1 + and 2 + fall within the normal range indicates, we believe, that the roentgen-ray findings have no bearing on the vital capacity measurements. These considerations make it possible to predict with reasonable confidence that apparently normal children revealing a vital capacity reading within normal limits will present, by roentgen ray, a normal picture according to currently accepted standards; and that children exhibiting a diminished vital capacity will show (other factors known to diminish the vital capacity being excluded) roentgenographic evidences of tracheobronchial adenopathy.

Our observations of the group with clinical symptoms and physical signs of tracheobronchial adenopathy are of interest in that they show a close relation between roentgen-ray findings, vital capacity and clinical diagnosis. The vital capacity measurement is of clinical significance, therefore, in that it affords corroborative evidence concerning the clinical course and the diagnosis. Of interest are the low individual vital capacity values observed in the group with symptoms of active infection. Though the number observed is too few for any final conclusions, these observations tend to indicate that a reduction of vital capacity in subjects with tracheobronchial adenopathy of more than 25 per cent. is suggestive of an active infection; while a reduction of vital capacity in similar subjects of from 15 to 25 per cent. is suggestive of a healed or latent infection. While in no way may the diminished vital capacity observed indicate the etiologic factor, these observations support the view that a reduction of vital capacity of more than 15 per cent. supplies corroborative diagnostic evidence of tracheobronchial adenopathy.

Since at the present time the pathology underlying the roentgen-ray findings observed is inconclusive, any explanation as to the diminished vital capacity observed is speculative. However, if we consider the shadows observed as caused by connective tissue changes, due to either tuberculous or nontuberculous infection, healed or active, it is reasonable to assume a loss of lung elasticity, which may be expected to reduce the vital capacity measurement. To substantiate this assumption, extensive observations controlled by careful necropsy would be necessary. Such a study is not possible in children, but it has seemed practical in animals, and we are undertaking such an investigation.

SUMMARY

1. Diminished vital capacity and roentgenologic evidence of tracheobronchial adenopathy were found in 16 per cent. of apparently normal white subjects, and 84 per cent. of apparently normal colored subjects.
2. A reduction of vital capacity of more than 15 per cent. in an apparently normal child indicates the necessity of a roentgenologic examination.
3. The possible presence of tracheobronchial adenopathy must be considered in the evaluation of the vital capacity measurement in apparently normal children.
4. A reduction of vital capacity of from 15 to 42 per cent. was found in children with tracheobronchial adenopathy.
5. The vital capacity is an aid in the diagnosis of tracheobronchial adenopathy.

CONGENITAL DEFECT OF THE SKIN OF THE NEW-BORN *

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Congenital defect of the skin constitutes one of the rare and interesting anomalies peculiar to the new-born infant. Recently, a striking example of the condition came under our observation, and in view of the vast extent of the skin defect present in this infant, together with the rarity of its occurrence, a report of the case seems desirable.

From the cases recorded in the literature, it is apparent that the lesions most frequently involve the scalp. They do occur, however, on the trunk and extremities, and in these locations the skin defects are often bilateral and also may be fairly symmetrical in their extent on the two sides of the body. The defects are present in early fetal life; thus they undoubtedly originate in utero. The margins of the involved areas are sharply defined and slightly elevated. Microscopic examination shows a failure in development, not only of the epidermis, but also of the glands, smooth muscle and adipose tissue of the skin. The presence of extensive defects of the skin is not incompatible with the life of the infant, and with proper treatment, areas of wide extent may heal spontaneously and without resort to skin grafts.

Various theories have been advanced to explain the cause of this interesting condition, but none are entirely satisfactory and convincing. In view of the uncertainty as to the etiology, we will content ourselves with a detailed report of the case.

REPORT OF CASE

Mrs. B., the mother of the baby having the extensive skin defect, was 31, and had been married five years. She was the mother of two healthy normal children. With her third and last pregnancy, the last menstrual period began July 28, and ended July 31, 1921. Life was first felt about November 7, 1921, and the expected date of confinement was April 8, 1922. On September 18, 1921, the mother underwent cholecystectomy, following which she promptly developed a marked jaundice associated with pale colored stools. After the operation, she had bearing down pains, with slight blood spotting, which lasted a few days.

The patient remained in a rather poor physical condition with low blood pressure, slight fever, rapid pulse, slight leukocytosis and continued jaundice, with bilirubin in the urine.

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* Received for publication, Nov. 7, 1923.

On account of her poor general condition, coupled with the persistent jaundice, labor was induced, Feb. 27, 1922, with the hope of securing a viable child, and also of alleviating the mother's condition by terminating the pregnancy. The course during the puerperium was fairly normal. There was some improvement in her general health and diminution in the jaundice, but the stools remained clay colored.

At birth, the baby weighed 1,610 gm. The placenta was small, round, friable and bright red, with a considerable area of degeneration present. The defect of the skin in this infant extended as a band 1.5 cm. wide across the anterior part of the abdomen above the umbilicus, and on the lateral sides of the trunk spread upward over the ribs and down to the crest of the ileum. The photograph (Fig. 1), taken March 8, 1922, or nine days after the birth of the infant, shows the extent and distribution of the skin defect on the left side of the body. A small area present on the lateral aspect of the arm, is not shown. At birth, the area was covered by a thin, delicate, translucent membrane, through which fine blood vessels, and also the ribs, were distinctly visible. Apparently, the muscles in these regions were also absent to some extent. Small skin defects about 2 by 3.5 cm. in size were also present on the lateral aspects of each thigh and arm. Linear scars running upward along the posterior axillary fold, and downward over the crest of the ileum connected these small areas with the large one on each side of the trunk, suggesting that at one time the skin defects may have been larger than at birth, and that some healing had occurred in utero. The symmetry of the extent and of the distribution of the lesions on the two sides of the body was striking.

Two days after birth, the thin membrane had broken down, and the area was covered by an opaque yellowish crust, from beneath which there was a slight oozing of serum. A few days later, the epithelium at the margins of the area became reddened and slightly thickened, and slowly began to replace the crust covering the area of the skin defect. The healing process steadily progressed in this manner, and about seventeen days after birth, the areas on the thighs and arms were completely covered by epithelium. When the baby was 2 months old, the large areas on each side of the trunk were also practically healed, except for a small region on each side about 1.5 cm. in diameter. Subsequently, the healing process progressed to completion, leaving slight scarring and retraction of the skin in the involved areas, as shown in Figure 2.

At first, the treatment consisted in dusting the area with a powder of equal parts of calomel and bismuth, over which sterile gauze dressing were applied. Because of a tendency for the gauze dressings to adhere to the crusts covering the lesion, we impregnated the gauze dressings with paraffin. This procedure obviated the difficulty we had encountered, and proved most satisfactory. With this treatment, the lesions healed completely and spontaneously, and without resort to skin grafts. The child is still living and in good health.

Instead of entering into a discussion of the literature dealing with this subject, we refer the readers to the complete bibliography published by Abt [1] in 1917. We wish, however, to point out the fact that the distribution of the skin defect in the case reported by Hahn [2] in 1841 greatly resembled that of the skin defect in our case.

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[1] Abt, I. A.: Congenital Skin Defects, Am. J. Dis. Child. **14:**113 (Aug.) 1917.

[2] Hahn: Angeborener Defekt eines grossen Theils der Haut des Rumpfes, J. d. Chir. u. Augenh. **30:**156, 1841.

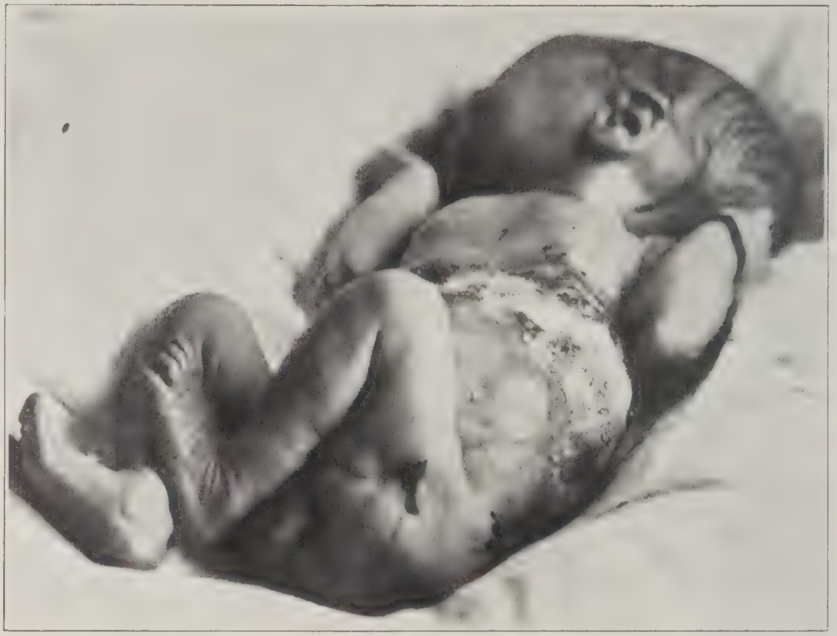

Fig. 1.—Appearance of child on the ninth day after birth, showing the extent and distribution of the skin defect on the left side of the body. A small area present on the lateral aspect of the arm is not shown.

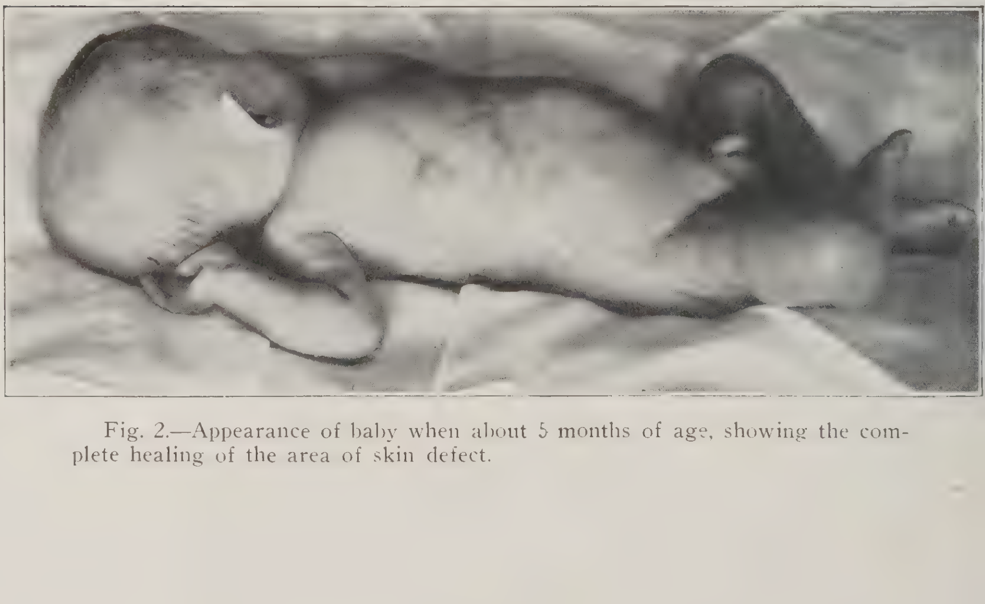

Fig. 2.—Appearance of baby when about 5 months of age, showing the complete healing of the area of skin defect.

SUMMARY

In the case of a new-born infant, which at birth had an extensive congenital defect of the skin, the symmetry of the lesions on the two sides of the body was striking.

The most satisfactory treatment consisted in dusting the region with powder composed of equal parts of calomel and bismuth, over which gauze dressings impregnated with paraffin were applied. With this treatment, complete healing occurred without resort to skin grafting.

AMINO-ACID CONTENT OF BLOOD OF INFANTS AND CHILDREN *

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Preliminary to beginning some studies on the amino-acid metabolism of infants and children, it was deemed advisable to obtain figures that would establish with reasonable accuracy the normal fasting amino-acid content of the blood. Owing to the comparatively short period of time that has elapsed since the development and introduction of the Folin method[1] of amino-acid determination, the literature, to date, contains no such observations for use as normal standards.

In the accompanying tables are submitted the results of studies made by the Folin method in fifty cases selected to range from infancy to puberty.

To carry on these observations, it was necessary to choose subjects already in the hospital. While these, of course, are hospital cases they are hospital normals so far as their selection can be controlled. Only patients whose convalescence was definitely established, in whom no kidney impairment existed and whose temperatures were normal were observed. They had been receiving for several days the usual diet for their age. The blood was obtained in the morning, with the subject fasting since the evening meal of the preceding day. In the case of infants, feedings were withheld for six hours.

Tables 1 and 2 give the findings in infants and children.

It has been found for infants and children that there is a variation from 3.92 to 7.14 mg. in 100 c.c. of normal fasting blood; with an average figure of 5.42 mg. per hundred cubic centimeters of blood. The fairly uniform values obtained throughout the periods of infancy and childhood show also that weight does not affect amino-acid values.

In addition to the amino-acid, determinations of the nonprotein nitrogen,[2] of the uric acid[3] and, on as many as possible, of the creatinin[2]

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* Received for publication, Sept. 27, 1923.

* From the Children's Medical Service Massachusetts General Hospital.

[1] Folin, D., and Wu, H.: System of Blood Analysis: New Colorimetric Method for Determination of Amino-Acid Nitrogen in Blood, J. Biol. Chem. **51**:377 (April) 1922.

[2] Folin, D., and Wu, H.: System of Blood Analysis: Methods for Analysis of N.P.N. and Creatinine, J. Biol. Chem. **38**:81 (May) 1919.

[3] Folin, D.: System of Blood Analysis: Revision of the Uric Acid Method, J. Biol. Chem. **54**:153 (Sept.) 1922.

TABLE 1.—*Determinations of Blood Amino-Acid Nitrogen* of Normal Infants*

Case	Age	Sex†	Amino-Acid	N. P. N.	Uric Acid	Creatinin	Diagnosis
1	9 da.	♂	6.02	30.3	2.80	1.13	G. C. conjunctivitis
2	14 da.	♀	5.04	20.1	1.60	....	Staph. conjunctivitis
3	16 da.	♂	6.93	20.4	3.32	....	Staph. conjunctivitis
4	21 da.	♀	6.65	19.8	2.32	....	?G. C. conjunctivitis
5	21 da.	♂	4.83	30.0	3.20	1.17	G. C. conjunctivitis
6	4 wk.	♂	5.95	19.2	4.44	....	G. C. conjunctivitis
7	6 wk.	♂	5.25	28.8	3.08	1.23	G. C. conjunctivitis
8	6 wk.	♀	5.39	30.6	2.56	0.87	G. C. conjunctivitis
9	8 wk.	♀	5.25	25.5	1.28	....	G. C. conjunctivitis
10	10 wk.	♀	5.53	30.3	....	....	G. C. conjunctivitis
11	11 wk.	♂	6.37	15.0	1.44	....	G. C. conjunctivitis
12	3 mo.	♂	4.41	19.8	1.50	0.96	Pyloric stenosis
13	5 mo.	♂	4.76	21.7	2.04	0.96	Bronchopneumonia
14	7 mo.	♂	5.67	25.2	1.80	1.81	Regulation feeding
15	7 mo.	♂	6.02	41.4	6.04	....	Fracture of femur
16	11 mo.	♀	5.95	26.4	3.16	1.28	Bronchopneumonia
17	13 mo.	♂	6.23	27.9	2.48	....	Cleft palate
18	20 mo.	♀	4.90	28.5	2.48	....	Lacerated lid o.d.
19	22 mo.	♂	4.90	37.5	6.76	....	Phlyctenular keratitis
20	22 mo.	♀	5.32	33.0	6.60	....	Phlyctenular keratitis
Maximum....................			6.93	41.4	6.76		
Minimum....................			4.41	15.0	1.28		
Average..................			5.57	26.6	3.10		

* Milligrams per hundred cubic centimeters of blood.

† In this column, ♀ indicates female, ♂ male.

TABLE 2.—*Determinations of blood Amino-Acid Nitrogen of Normal Children*

Case	Age, Years	Sex	Amino-Acid	N. P. N.	Uric Acid	Creatinin	Diagnosis
21	2	♂	4.48	28.8	4.84	....	Rickets
22	3	♂	4.69	27.6	4.04	....	Congenital syphilis
23	3	♂	4.90	30.9	3.20	1.08	Prolapse of rectum
24	4	♂	4.83	22.8	3.48	....	Impetiginous keratitis
25	4	♀	5.04	30.6	3.04	....	Otitis media
26	4	♀	5.46	25.8	2.84	....	Mastoiditis
27	4	♂	5.04	32.1	5.16	....	Acute arthritis
28	4	♂	5.32	29.1	3.28	1.09	Mastoiditis
29	4	♂	5.67	26.7	2.88	....	Postaural abscess
30	5	♂	5.74	49.5	5.88	1.29	Esophagoscopy
31	5	♂	5.88	26.7	4.24	....	Chronic endocarditis
32	5	♀	5.53	27.9	4.16	....	Mastoiditis
33	7	♂	5.74	25.5	4.16	....	Pleural effusion
34	8	♀	4.76	30.3	3.16	1.05	Brachial cyst
35	8	♀	6.09	32.4	4.64	1.18	Phlyctenular keratitis
36	8	♂	5.56	24.0	3.32	....	Mastoiditis
37	8	♂	3.92	27.3	2.56	1.19	Fractured femur
38	9	♂	4.90	28.2	....	....	Mastoiditis
39	9	♂	5.60	25.4	4.00	....	Mastoiditis
40	10	♂	5.18	25.4	4.80	....	Mastoiditis
41	11	♂	5.67	31.2	2.92	....	Chorea
42	11	♂	4.69	30.3	5.08	....	Contracted orbit o.d.
43	11	♂	4.48	24.9	3.96	....	Traumatic eye
44	12	♂	5.18	27.9	3.20	....	Hypopyon ulcer o.s.
45	12	♀	4.90	27.3	4.40	....	Phlyctenular keratitis
46	12	♀	5.74	25.1	2.96	....	Hair lip; cleft palate
47	13	♂	7.14	....	3.60	....	Endocarditis
48	13	♂	4.69	24.6	3.24	....	Fractured femur
49	14	♂	5.74	22.7	3.56	....	Mastoiditis
50	15	♂	5.95	28.2	....	....	Mastoiditis
Maximum....................			7.14	49.5	5.88		
Minimum....................			3.92	22.7	2.56		
Average..................			5.28	28.2	3.80		

were made for sake of comparison and as a further check on the normalcy of the group.

In Table 3 are given the findings in a series of normal adults (physicians and research assistants in the Massachusetts General Hospital). These determinations were made for the sake of comparing results obtained in these adults with the same technic and solutions as were used for the infants and children, also for comparison with results reported in adults by Professor Folin [4] and a larger unpublished series by Cobb, Lennox and O'Connor.

In Folin's series of twelve young men, he found a maximum value of 7.8 mg. and a minimum of 5.7 mg., with an average of 6.4 mg.; a slightly lower figure than that obtained by us.

The figures of Cobb, Lennox and O'Connor correspond more closely to those given in Table 3.

Table 3.—*Determinations of Blood Amino-Acid Nitrogen of Normal Adults*

Case	Age, Years	Sex	Amino-Acid	N. P. N.	Uric Acid	Creatinin
1	30	♂	8.12	33.6	4.68	1.40
2	24	♀	6.79	29.7	4.16	1.32
3	29	♂	7.56	30.3	4.28	1.47
4	27	♀	6.36	27.6	3.68	1.40
5	31	♂	7.35	28.8	3.72	1.28
6	25	♀	6.51	27.6	3.28	....
7	27	♂	6.94	29.8	4.75	1.53
8	24	♂	7.28	33.3	3.60	1.26
9	28	♂	6.44	34.2	4.28	1.34
Maximum			8.12	34.2	4.75	1.53
Minimum			6.36	27.6	3.28	1.26
Average			7.04	30.5	4.05	1.37

The figures presented show that while age plays no great part in the amino-acid blood content in the group here considered, during infancy and childhood the average amount present is lower than that for adults.

A number of observations obtained in children with definite organic disease showed distinct deviations from the normal range.

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[4] Folin, D., and Berglund, H.: Retention and Distribution of Amino-Acids with Special Reference to Urea, J. Biol. Chem. **51**:395 (April) 1922.

REVIEW OF THE LITERATURE FOR 1921 AND 1922 ON NEUROLOGY OF CHILDREN *

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MENINGES

A number of new symptoms, some of them observed by Brudzinski in irritative and inflammatory processes of the meninges, have been described by Jonscher;[1] for instance, flexion of the contralateral extremity following pressure on the upper arm or thigh, and a contralateral reflex on flexion of one arm. They are referred to hyperalgesia and, as the well known neck phenomenon of Brudzinski, are genetically brought in relation with the altered state of body colloids.

Meningitis in infancy is rather infrequent, especially under 3 months of age; and then it is caused by certain micro-organisms that rarely play a rôle later. J. V. Cooke and H. H. Bell,[2] in reviewing the literature of the last five years, encountered only twelve cases of meningococcus meningitis in infants under 3 months of age. In a series of 218 cases of tuberculous meningitis in children under 3 years of age, only three infants, and among 104 children with influenzal meningitis only ten, were under 3 months old. Cases of streptococcus, staphylococcus and pneumococcus meningitis are more frequent. Apparently peculiar to the very young are infections with colon bacilli and allied intestinal bacteria; aerogenes bacteria, *B. mucosus-capsulatus, B. pyocyaneous* and *B. typhosus*. The authors add their own observations of meningitis in early infancy due to a bacillus belonging to the paracolon group and due to the bacterium elasticum, hitherto undescribed. Greenthal[3] observed purulent meningitis, caused by *Bacillus acidi-lactici,* in an infant 1 month old, and Sherman[4] observed this condition in a new-born infant. Smith and Aberd[5] isolated the bacterium enteritidis in a case, and Miller and Lyon,[6] a threadlike diphtheroid micro-organism.

Influenzal Meningitis.—Influenzal meningitis is obviously a disease of infancy. This becomes evident from various statistics relative to the incidence of the affection. The study of 692 cases of purulent

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* Received for publication, Oct. 6, 1923.

[1] Jonscher, K.: Pedjatrja pol **2**, 1922, abstr. Jahrb. f. Kinderh. **49**:175, 1922; and Monatschr. f. Kinderh. **24**:377, 1922.

[2] Cooke, J. V., and Bell, H. H.: Incidence of Meningitis in Early Infancy, Am. J. Dis. Child. **24**:387 (Nov.) 1922.

[3] Greenthal, R. M.: Case of Meningitis Due to Bacillus Acid-Lactic, Am. J. Dis. Child. **21**:203 (Feb.) 1921.

[4] Sherman: Tr. Am. Pediat. Soc. **34**:192, 1922.

[5] Smith, John, and Aberd, M. B.: Lancet **2**:705 (Oct.) 1921.

[6] Miller, M. K., and Lyon, M. W., Jr.: Am. J. M. Sc. **162**:593 (Oct.) 1921.

meningitis carried out by the department of health of New York City during the past ten years and published by Josephine B. Neal[7] revealed that, among the thirty-two influenza patients, only two were more than 5 years old and sixteen were children of 1 year or less. T. M. Rivers,[8] who reviews 197 cases of various writers and reports twenty-three new cases, found that 79 per cent. of cases occurred in children under 2 years of age. The mortality among 220 patients was 92 per cent. He remarks that no clinical signs were peculiar to influenzal meningitis, so that, especially in infants, undoubtedly the disease escaped recognition, having been mostly mistaken for pneumonia. Smears of the spinal fluid practically always showed gram-negative pleomorphic bacilli. Blindness, paralysis and deafness were the usual sequels. In the majority of cases, the meningitis was possibly a primary disease, produced by a strain of influenza bacilli closely allied to each other but differing from the ordinary respiratory strains. At times, it was secondary, and was caused by the ordinary respiratory strains.

An instance of influenzal meningitis (without necropsy) has been closely studied by Abt and Tumpeer.[9]

Meningococcus Meningitis.—Whenever the fluid obtained by lumbar puncture is clear in suspected meningococcus meningitis, injection of 5 to 10 c.c. of antimeningococcus serum is recommended by Sainton and Schulmann.[10] This is said to be liable to transform the clear fluid into the usual purulent fluid within a few hours by inducing an influx of leukocytes and meningococci.

Among twelve children, all under 3 years, with epidemic meningitis, observed by Squarti,[11] the mortality was 58 per cent. The author emphasizes that the disease may occur in fulminating form so that the sudden death may have medicolegal importance, and that there exists also a pseudotyphoid, a walking and an ephemeral masked form with variable evanescent symptoms. In one of the four atypical cases, a child was convalescent from typhoid when the meningitis developed, and both the typhoid bacillus and the meningococcus were isolated in the spinal fluid.

Root[12] reports the second case known to literature of meningococcus meningitis at the age of 5 weeks, probably acquired at birth, with obstructive hydrocephalus during the acute stage.

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[7] Neal, Josephine B.: Arch. Pediat. **38**:1 (Jan.) 1921.

[8] Rivers, T. M.: Influenzal Meningitis, Am. J. Dis. Child. **24**:102 (Aug.) 1922.

[9] Abt, I. A., and Tumpeer, I. H.: Influenzal Meningitis, Am. J. Dis. Child. **21**:444 (May) 1921.

[10] Sainton, P., and Schulmann, E.: Bull. méd., Paris **35**:465 (June) 1921; abstr. J. A. M. A. **77**:323 (July 23) 1921.

[11] Squarti, G.: Pediatria **30**:198 (March) 1922; abstr. J. A. M. A. **78**:1426 (May 6) 1922.

[12] Root, J. H.: Meningococcus Meningitis with Obstructive Hydrocephalus in the Newly-Born, Am. J. Dis. Child. **21**:500 (May) 1921.

Lewkowicz [13] offers evidences that meningococcus infection takes place through the choroid plexus, so that the inflammatory process develops first in the ventricles and spreads from here to the subarachnoid spaces. Woringer's [14] two cases support this assumption. The logical treatment in case of block would be intraventricular injection of specific serum. Howell and Cohen [15] recommend intraventricular, and in certain conditions, subdural treatment in meningococcus meningitis. One of the factors responsible for the still too high mortality rate and incidence of sequels, even with careful intraspinal injections, is the failure of the serum to reach the foci of inflammation because of the basilar arachnoid spaces being shut off from those above, because of the closure of the small formina of Magendi and Luschka by inflammation or by sagging, the inflammation of the ventricles and the formation of pockets over the cortex of the brain. The serum, therefore, must be introduced above the block and flow over the affected areas. Howell and Cohen, who since 1914 have given early intraventricular injections of serum to infants, have obtained encouraging results. In some cases, the introduction of serum subdurally at the outer edge of the fontanel has yielded marvelous results, and evidently the foci have been reached.

The efficacy of the intraspinal injections has been again attested to, lately, by Nebendahl,[16] who, among twelve cases so treated, had a mortality of 30 per cent., which compares very favorably with the high mortality of 80 per cent. among a small group treated without antitoxin.

Mitchell and Reilly [17] report meningococcus meningitis in a 4-months-old infant, cured by cistern puncture. Heist and Cohen [18] present evidence that the spinal fluid strains of meningococci are much more virulent for men than are the carrier strains.

The often striking difference between the severity of the clinical picture and the degree of infection or the number of meningococci in the lumbar puncture fluid is explained by Shearer and Parson [19] by the degree of acidosis of spinal fluid. A subnormal quantity of substances from which the cocci form acid or the presence of a strain of organisms less capable of producing the usual amount of acid may account for

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13. Lewkowicz, K.: Arch. de méd. d. enf. **24:***329*, 407, 549, 1921.
14. Woringer, P.: Arch. de méd. d. enf. **24:**159 (March) 1921.
15. Howell, W. W., and Cohen, S. A.: Intraventricular and Subdural Serum Treatment of Meningococcus Meningitis in Infancy, Am. J. Dis. Child. **24:**427 (Nov.) 1922.
16. Nebendahl: Arch. f. Kinderh. **71:**294 (Aug.) 1922.
17. Mitchell, A. G., and Reilly, J. J.: Am. J. M. Sc. **164:**66 (July) 1922.
18. Heist, G. D.; Cohen, S. S., and Cohen, M. S: J. Immunol **7:**1 (Jan.) 1922.
19. Shearer, C., and Parson, T. R.: Quart. J. Med. **14:**120 (Jan.) 1921.

the slight change in reaction of the patient's spinal fluid, even in the presence of a great number of meningococci; and, thus, for the mild clinical course.

Various Other Forms of Meningitis.—Strains of parameningococcus were isolated by Monserrat[20] in two sporadic cases and Cicszynski[21] describes purulent meningitis caused by typhoid bacillus, with entirely clear lumbar puncture fluid. Neumann and Kempner[22] and Fonzo[23] saw fatal meningitis due to streptotrix. The same micro-organism gave rise to a granulomatous tumor of the pons in a girl, reported by Zibordi.[24]

The presence of Kernig's sign in a surprisingly large proportion of infants and children with ordinary acute infections of nose and throat is interpreted by Göppert[25] as evidence of some involvement of the meninges, which may explain the restlessness or apathy of the patient. Loewy,[26] after studying 350 cases of serous meningitis with 425 lumbar punctures, confirmed the fact that the spinal fluid under normal conditions is a secretion, but in disease has more the character of a filtrate. The term serous meningitis expresses too much in some cases and not enough in others. In all infectious diseases with disturbances of the nervous system, acute serous meningitis is present, ranging from a mere toxic irritation of the vessels to infiltration of the pia, recognizable by lumbar puncture with proper interpretation.

Meningitis as a manifestation of mumps infection, although almost unknown in Buenos Aires, is rather common in Montevideo, not far away, according to reports of Morquis.[27] He observed a number of cases in which the meningitis preceded, accompanied or followed the parotitis; and in some instances meningitis was the only manifestation of the infection. Complete recovery was the rule, though sometimes deafness followed.

Tuberculous Meningitis.—The respiratory anomalies in tuberculous meningitis were studied by Eckstein and Rominger.[28] One group is due to the general miliary dissemination with its pulmonary and hematogenic factor. The other has its origin in the cerebrospinal

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20. Monserrat, C.: J. Philippine Islands M. A. **2**:15 (Jan.-Feb.) 1922.

21. Cicszynski, F. K.: Pedjatrja Pol. **2,** 1922.

22. Neumann, R., and Kempner, L. R.: Ztschr. f. klin. med. **94**:215 (June) 1922.

23. Fonzo, F.: Pediatria **30**:1045, 1922.

24. Zibordi, F.: Clin. Pediat. **3**:1, 1921.

25. Göppert: Klin. Wchnschr. **1**:64 (Jan. 8) 1922; abstr. **78**:930 (March 25) 1922.

26. Loewy, R.: Wien. Arch. f. inn. Med. **4**:305, 1922; abstr. J. A. M. A. **79**:1888 (Nov. 25) 1922.

27. Morquis, L.: An. de Fac. de med., Montevides **7**:23 (March-April) 1922.

28. Eckstein, A., and Rominger, E.: Arch. f. Kinderh. **70**:258 (Jan.) 1922.

affection itself and results from (1) irritation; (2) reflectoric inhibition, or (3) partial or total paralysis of the respiratory center. The manifestations consist in alterations of frequency and rhythm. They occur with a certain regularity in all three stages, especially at the end of the second and during the entire third stage. The first sign is the appearance of yawning and sighing; then follows acceleration, the irritative form, which changes into the periodic form, until this becomes of the Cheyne-Stokes type. These disturbances present a dissociation of the respiration on a functional basis.

A rare case of tuberculous meningitis with marked thickening of the spinal meninges from a diffuse infiltration with tubercles, extending from the cervical to the lumbar region, is reported by Regan and Cheney.[29] The findings explained the failure to obtain any spinal fluid by lumbar puncture.

The value of Binda's shoulder sign for the early recognition of tuberculous meningitis has been confirmed by Tronconi.[30] The sign consists of a sudden movement of the shoulder when the head is briskly turned passively to the other side. Harbitz,[31] writing on the curability of tuberculous meningitis, points to the interesting fact that, while about 60 per cent. of all cases occur in the first two years of life and quite regularly result in death, the cases of recovery have occurred in older children and adults. Cramer and Bickel,[32] who report a recovery from this disease in a young man of 19, collected forty-four cases of recovery, in which 30 per cent. of the patients were over 20 and 2.5 per cent. under 2½ years of age.

In two cases a specific reaction, resulting from intradermal injection of the patient's own cerebrospinal fluid, was obtained by Korbsch.[33]

Artificial Pneumorachis.—Zorrillo y Polanco [34] thinks that subcutaneous injection of cerebrospinal fluid drawn by lumbar puncture, supplemented with injections of warm air into the spinal canal, may improve the prognosis of tuberculous meningitis. Injection of air or oxygen into the subarachnoid space by means of lumbar puncture was used by Sharp [35] in a few cases of epidemic meningitis, to render the evacuation of cerebrospinal fluid possible by mechanically breaking up secluded

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29. Regan, J. C., and Cheney, G. W. H.: Tuberculous Meningitis with Dry Spinal Subarachnoid Due to Diffuse Tubercle Infiltration of Spinal Meninges, Am. J. Dis. Child. **22**:516 (Nov.) 1921.

30. Tronconi, S.: Pediatria, Naples **29**:802 (Sept.) 1921.

31. Harbitz, F.: Am. J. M. Sc. **161**:212 (Feb.) 1921.

32. Cramer, A., and Bickel, G.: Ann. de méd. **12**:226 (Sept.) 1922.

33. Korbsch, R.: Med. Klin. **17**:816 (July 3) 1921.

34. Zorrillo y Polanco, A.: Arch. españ. de pediat. **6**:462 (Aug.) 1922; abstr. J. A. M. A. **79**:2198 (Dec. 23) 1922.

35. Sharp, E. A.: Artificial Pneumorachis in Treatment of Acute Infections of Meninges, Arch. Neurol. & Psychiat. **6**:669 (Dec.) 1921.

pockets, or to drive out superfluous fluid before injecting serum. The results in sixty-four cases of various forms of meningitis justify a hopeful outlook for this class of meningococcus infection, in the opinion of the author.

HYDROCEPHALUS

As the cerebrospinal fluid, similarly to the blood or lymph, circulates in a closed vascular system, flowing from the ventricles through the foramina of Magendie and Luschka as the only paths of communication into the subarachnoid spaces of the cerebral sulci, where almost all of it is absorbed, an obstruction of the ventricles or of the larger subarachnoid spaces, the cisternae, must result in hydrocephalus; in the first case of the obstructive, in the latter of the communicative type. Dandy [36] holds it possible that hydrocephalus manifested soon after birth may be due to failure of the foramina to develop, or to intra-uterine or postnatal inflammation. Adhesions following meningitis by occluding the cisternae are the most common cause of the communicative type. In every instance, the diagnosis of hydrocephalus and the exact site and character of obstruction can be determined by ventriculography and the phenolsulphonephthalein test, and the lesion can always be found at operation. The only satisfactory treatment of hydrocephalus is by attacking its cause directly; for instance by construction of a new foramen of Magendie. A similar attitude is maintained by Litchfield and Dembo,[37] who feel that the rôle of the endocrines in the hypersecretive form, while as yet indefinite, looms as a significant factor. The value of ventriculography for the differentiation of the type of hydrocephalus was demonstrated by E. B. Towne [38] in three cases. One of them presented the rare condition of unilateral obstructive hydrocephalus. The tendency of hydrocephalus in chondrodystrophia to spontaneous cessation of increase has been stressed by Dandy,[39] who attempts to explain this form by certain bone anomalies in the base of the skull, which during the process of growth disappear, the cause of hydrocephalus thus being eliminated.

Intravenous injections of a strongly hypertonic saline solution caused a brief initial rise of the intraventricular pressure, followed by marked depression in cats, in which Nañagas [40] had produced artificial hydrocephalus by injecting a suspension of lampblack into the lateral ventricles or into the cisterna cerebellomedullaris. This depression was possibly due to a rapid resorption of cerebrospinal fluid. Hypotonic fluids (distilled water) had the opposite effect. He also demonstrated that the absorption takes place through the ependymal into the underlying capillary network. The choroid plexus does not participate in this process. Wislocki and Putnam,[41] in their animal experiments, came to identical conclusions relative to absorption.

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[36] Dandy, W. E.: Surg. Gynec. & Obst. **32:**112 (Feb.) 1921; Bull. Johns Hopkins Hosp. **32:**67 (March) 1921.

[37] Litchfield, H. R., and Dembo, L. H.: Clinical and Therapeutic Aspects of Chronic Internal Hydrocephalus, J. A. M. A. **78:**711 (March 11) 1922.

[38] Towne, E. B.: Value of Ventriculograms in Localization of Intracranial Lesions, Arch. Surg. **5:**144 (July) 1922.

[39] Dandy, W. E.: Bull. Johns Hopkins Hosp. **32:**5 (Jan.) 1921.

[40] Nañagas, J. C.: Bull. Johns Hopkins Hosp. **32:**381 (Dec.) 1921.

The production and absorption of the cerebrospinal fluid, etiologic pathology, symptomatology, ventriculography, principles of treatment and technic of operation are discussed in detail by Fraser and Dott.[42] In five cases of the extraventricular type, they have, by ligature of the common carotids, achieved promising results. Among thirteen cases of the ventricular variety, apparent arrest of the affection resulted from surgery in three instances, and a complete cure in two cases.

Cassel[43] found the prognosis of syphilitic hydrocephalus as a rule unfavorable despite energetic antisyphilitic treatment, as most patients retain more or less mental defects, and others become markedly neuropathic. Nevertheless, he urges energetic specific therapy in every case.

The pseudohydrocephalic complex in prematurely born infants, termed by Ylppoe megalocephalus, has been discussed by Rosenstern[44] in a paper on the secondary stigmata of prematurely born infants. He argues that the disproportion between the large head and the small body is due to an increase of the brain volume faster than that of the capacity of the skull. The intraspinal pressure was in every instance increased, but in no case did he find hydrocephalus in the postmortem examination. Megalocephalus is a partial manifestation of the peculiar somatic and psychic habitus of prematurely born infants, and is probably due to imperfection of their endocrine system and the premature loss of maternal hormones.

DEFECTIVE DEVELOPMENT

An elaborate work on the morphology of microcephaly has been contributed by Patane.[45] He gives exact craniometric data and a special description of the lower jaw of a 19-year-old microcephalic idiot with spastic tetraplegia, typical contractures, epilepsy and a marked development of lanugo. The principal features of the brain were porencephaly, microcephaly, simple hypotrophy, hydrocephalus (*ex vacuo*), atrophy of the corpus callosum and hypoplasia of the pyramidal tracts. The atrophic parts seem to be the site of the primary disturbance, the

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41. Wislocki, G. B., and Putnam, T. J.: Am. J. Anat. **29**:313 (Sept.) 1921.
42. Fraser, J., and Dott, N. M.: Brit. J. Surg. **10**:165 (Oct.) 1922.
43. Cassel: Deutschr. med. Wchnschr. **48**:655 (May 19) 1922.
44. Rosenstern, J.: Ztschr. f. Kinderh. **32**:129 (April) 1922.
45. Patane, M.: Riv. di antrop. **24**:209, 1921.

hypotrophic ones being probably associated areas, depending on the former. The microgyria is considered as due to inflammatory processes. Interesting conclusions are made as to the development of the fissura Sylvii, and, in the assumption of certain laws of development, as to a mutual influence of adjacent parts.

Partial absence of the corpus callosum in a 15-year-old idiot is described by Cameron and Nicholls,[46] with a detailed clinical picture and complete necropsy report; and congenital hydranencephaly due to inflammatory processes and abnormalties of the vascular "anlage" with an almost complete absence of brain and midbrain in an intact skull by Licen.[47]

Young[48] reports in full two acrocephalic cases, and after a review of the various conjectures relative to the etiology, argues in favor of dysendocrinism dating from the blastoma stage being the basis of the condition. Weygandt,[49] in a minority of cases of oxycephaly, found weakmindedness or degenerative features and psychotic symptoms.

Blechmann[50] cites two cases of homalopsia exophthalmica, a congenital dystrophy of the skull, possibly of syphilitic origin, and characterized by a markedly flattened face, retraction of the bridge of nose, deformity of the palate and exophthalmus. The anomaly is associated with retarded dentition and psychic defects, and has a certain resemblance to mongolian idiocy and scaphocephalus. Apert classifies the condition among the syndromes of craniosynostosis, an anomaly of cranial ossification.

A spheno-orbital meningocele in a 2-year-old boy, of the size of the child's head, has been reported by Lutz.[51] Death from meningitis followed operation. The author compares with this the cases of facial encephalocele on record. The mortality ranged from 20 to 31 per cent. Intranasal transsphenoid encephalocele in a boy of 6 is described by Nager.[52] Death resulted one year later from streptococcus meningitis. The author was able to find only six analogous instances on record. A dicephalus is described by Beach.[53]

A contribution to the etiologic problem of porencephalus is offered by Globus.[54] He gives a detailed histopathologic description, with numerous illustrations of the porencephalic brain of an 11-months-old child. The defect proved to be due to meningo-encephalitis, leading to strangulation of the blood vessels with subsequent sclerotic changes. The findings are important in relation to the pathology of disseminated sclerosis.

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[46] Cameron, J., and Nicholls, A. G.: Canadian M. A. J. **11**:448 (June) 1921.

[47] Licen, E.: Ztschr. f. ges. Neurol. u. Psych. **64**:282, 1921.

[48] Young, F. W.: Arch. Pediat. **39**:629 (Oct.) 1922.

[49] Weygandt: Deutsch. Ztschr. g. Nervenh. **68-69**:495, 1921.

[50] Blechmann, G.: Bull. Soc. de pédiat. de Paris **9**:403, 1922.

[51] Lutz, F.: Brazil-med. **35**:17 (Jan. 8) 1921; abstr. J. A. M. A. **76**:899 (March 26) 1921.

[52] Nager, F. R.: Schweiz. med. Wchnschr. **52**:516 (May 25) 1922.

[53] Beach, W. M.: Case of Diredydimus (Dicephalus), J. A. M. A. **76**:1748 (June 18) 1921.

[54] Globus, J. H. B.: Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

Spina Bifida.—The roentgenographic examination of the vertebra and its congenital anomalies in the lumbosacral region is important and has revealed a great number of conditions hardly suspected. Hintze,[55] in a classic paper, deals with the relation of the normal sacral fontanel (fontanella lumbosacralis) to the pathologic spina bifida occulta and their differentiation in the roentgenogram. He details the findings in 150 skeletons of anthropoid apes; 400 human sacrums and lumbar vertebrae, and the roentgenograms of 700 others. He discusses the observations on the symptom complex of lumbosacral hypertrichosis, neuroparalytic disturbances in the lower extremities and vertebral hiatus (morbus diaboli) and myelodysplasia (Fuchs).

The anatomicopathologic conditions in spina bifida occulta which bring on progressive deformities of the feet, with a tendency in the majority of cases toward the development of pes equinus, varus, excavatus and their variations and combinations, as well as the principles of treatment, are dealt with by Roeren.[56] There are certain features in the minute structure in spina bifida that have a direct bearing on operative procedures, on prognosis as regards nervous function after and apart from operation; these have been detailed by Keiller.[57]

The remarkable occurrence of some degree of spinal defect in four children has been recorded by Pybus,[58] namely, spina bifida, spina bifida occulta, meningomyelocele in the sacral region and an exaggerated postanal dimple.

Valuable data relative to the frequency of heredofamilial defects, various localizations, types, cord involvement, clinical signs and operative results are presented by Woltman,[59] who reviews 187 cases of spina bifida, including three cases of myelodysplasia without bone defects. The opinions relative to the rôle spinal malformations, especially spina bifida occulta, play as factors in enuresis are still contradictory. That an anatomic basis for enuresis is not so rare as supposed is claimed by Sironi and Sabatini.[60] In their series of twenty cases of enuresis in children, in sixteen the fifth vertebra was deformed or there was spina bifida; and in one case the fifth vertebra and the sacrum had separated. In some, there was also myelodysplasia. No deformities of this kind were encountered in other children, free from enuresis. Peritz, quoted by Woltman,[59] has found 68 per cent. of spina bifida occulta among twenty-two adults with enuresis and 35 per cent. of spina bifida among twenty-two children with enuresis. Systematic studies by Altschul[61] of vertebrae of patients with enuresis revealed, in about three-fourths of the cases, anomalies of vertebrae. A number of rare malformations were discovered, as various types of lateral fissures, defects of the corpus vertebrae, spina bifida anterior, supernumerous rudiments and wedge-shaped vertebrae with supernumerary ribs. Chute[62] thinks that spina bifida occulta may explain a number of perplexing bladder disturbances. Operations have, on the whole, not been very satisfactory. The outlook, he states, would probably be more hopeful, if the operation were to be performed earlier.

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[55] Hintze, A.: Arch. f. klin. Chir. **119**:409 (April) 1922.

[56] Roeren, L.: Arch. f. orthop. Unfallschir. **19**:1-49, 1921.

[57] Keiller, Violet H.: Brain **45**:31 (June) 1922

[58] Pybus, F. C.: Lancet **2**:599 (Sept. 17) 1921.

[59] Woltman, H. W.: Minnesota Med. **4**:244 (April) 1921.

[60] Sironi, L., and Sabatini, L.: Riv. di clin. pediat. **20**:399 (July) 1922; abstr., J. A. M. A. **79**:1644 (Nov. 4) 1922.

On the other hand, Bonsmann,[63] who found spina bifida not only in families with enuresis but also in healthy families, failed to establish a connection between anomalies of vertebra and enuresis; and Gelpke[64] opposes Fuch's attempt to bring enuresis in an etiologic relationship to myelodysplasia.

Two cases of agenesis (congenital paralysis) of cranial nerves are reported by Cadwalader.[65]

Morgan and Stuart[66] report Oppenheim's disease in a boy of 9, in whom the weakness was limited to the lower extremities, with a tendency to marked improvement. They state that approximately 125 instances have been reported in the twenty years since Oppenheim described the affection. Some authors assume a close relationship between Oppenheim's disease and Werdnig-Hoffmann's affection. Leenhardt and Sentis,[67] for instance, who review the literature on these anomalies and analyze two of their own clinical observations, conclude that these diseases may be of the same nature and should be included under the nosologic term of diffuse chronic poliomyelitis of early infancy. In a contribution to the problem of the so-called congenital encephalitis of Virchow, stressing the subject of cortical and medullary encephalomalacia and sclerosis, Wohlwill[68] describes minutely nine cases, and

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61. Altschul, W.: Fortsh. a. d. geb. d. Roentgenstrahl. **27**:607, 1921.

62. Chute, A. L.: J. Urol. **5**:317 (April) 1921.

63. Bonsmann, M. R.: Deutsch. Ztschr. f. Nervenh. **74**:343, 1921.

64. Gelpke, H.: Monatschr. f. Kinderh. **19**:137 (Nov.) 1921.

65. Cadwalader, W. B.: Am. J. M. Sc. **163**:744 (May) 1922.

66. Morgan, W. G., and Stuart, D. D. V., Jr.: Amytonia Congenital Complicated by Acute Cholecystitis of Typhoid Origin, J. A. M. A. **78**:1105 (April 15) 1922.

67. Leenhardt and Sentis: Arch. de méd. d. enf. **24**:137 (March) 1921.

68. Wohlwill: Ztschr. f. ges. Neurol. u. Psychiat. **73**:360, 1921.

comes to the conclusion, arrived at also by Schwartz,[69] that Virchow's interstital congenital encephalitis cannot be considered encephalitis in the strict sense of the term.

Comby [70] relates his experiences with sixty-two cases in children suffering from acute encephalitis in connecetion with influenza, whooping cough, enteritis, measles and syphilis or from forms apparently having no connection with any other disease; and reviews the wide range of the symptoms. Recovery without sequelae ensued in one third of his cases.

Griffith [71] analyzes thirty-one cases of acute cerebellar encephalitis with two necropsies. In one fourth of the cases, there were signs of mental defects.

Hemorrhagic encephalitis following appendicitis with fibropurulent peritonitis recurred about ten years later in connection with influenzal pneumonia in a boy whose case is reported by Heusser.[72] These two successive brain processes were found in postmortem examination.

LETHARGIC OR EPIDEMIC ENCEPHALITIS

No single topic in the field of neurology has in the past few years received more attention than epidemic encephalitis and its sequelae. Only papers dealing with the disease in childhood can be covered in this brief review, though others will be given a passing consideration.

In the 274 cases studied by Josephine B. Neal [73] half of the patients were 15 years of age or younger; and 50 per cent. more boys were affected than girls, as is the case in epidemic meningitis and poliomyelitis. The symptoms in children did not differ greatly from those in the adults; the onset was more frequently sudden and the course ordinarily shorter than in the adults. In addition to the symptoms of infection, such as fever, headache, vomiting, constipation and malaise, those directly referable to the central nervous system showed an almost endless variety, comprising lethargy or insomnia, convulsions, ocular disturbances, paralyses of wide distribution, especially of the cranial nerves, disturbances of speech, twitchings, tremor, choreiform movements, catatonia, various changes in reflexes, and also in the Babinski's sign, and ankle clonus and profuse sweating. Typical meningeal signs were not common. The mortality in her series was 28 per cent.

Two well defined periods of the affection are distinguished: the acute stage and the sequelae. The polymorphous clinical pictures of the first stage are classified by Hofstadt[74] in the following groups: (1) the pure encephalitic types with a choreic, myoclonic, lethargic and choreic-athetotic subform; (2) the type resembling Landry's paralysis, with fatal issue; (3) the meningeal form, with typical meningeal symptoms; (4) the myelitic form; (5) the frequent abortive forms, under the mask of a slight "grippal" infection. Such abortive cases are especially discussed by Wallgren,[75] and two ambulatory cases are discussed by Williams.[76]

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[69] Schwartz: Ztschr. f. Kinderh. **29**:102; **31**:51, 1921.

[70] Comby, J.: Arch. de méd. d. enf. **24**:457, 488 (Aug.) 1921.

[71] Griffith, J. P. C.: Am. J. M. Sc. **162**:781 (Dec.) 1921.

[72] Heusser, H.: Deutsch. Ztschr. f. Nervenh. **71**:210, 1921.

[73] Neal, Josephine B.: Experience with More than 100 Cases of Epidemic Encephalitis in Children, J. A. M. A. **77**:121 (July 9) 1921.

With the wide range of and the manifold combinations in the symptomatology, the differential diagnosis, as discussed by Barker[77] minutely, may include a number of infections and intoxications, which simulate this disease: syndromes due to vascular lesions, intracranial neoplasms, chorea. parkinsonian disease, cataleptic and catatonic states, myasthenia gravis, progressive muscular atrophy, hysteria and neurasthenia. Yet despite the numerous clinical forms, the somnolent-ophthalmoplegic, the paralytic, amyostatic and hyperkinetic pictures are the commonest.

Two other important inflammatory, nonsuppurative diseases of the central nervous system which have certain features in common, namely syphilis and poliomyelitis, may give rise to occasional difficulties in differentiation. Bassoe[78] points to the apparent existence in encephalitis (as in syphilis) of a para stage, a progressive cerebral process coming on sometimes long after the acute illness, the virus giving rise to chronic and degenerative processes.

An interval as long as one and one-half years between the acute stage and recurrence is reported by Price;[79] and recrudescence after one year is reported by Blakeslee.[80]

An extremely malignant, rapidly spreading ward epidemic has been observed by Duzar and Baló[81] in which eleven babies contracted the disease. Nine died, of whom seven were examined postmortem. There were symptoms similar to those in alimentary intoxication, fever, convulsions, jactitation, disturbances of the sensorium, toxic respiration, hypertonia and ocular symptoms, the diagnosis proving very difficult clinically. The resemblance to severe alimentary intoxication in infants

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74. Hofstadt, F.: Ztschr. f. Kinderh. **29**:190 (June) 1921.

75. Wallgren, A.: Deutschr. med. Wchnschr. **47**:1053 (Sept. 8) 1921.

76. Williams, C. E.: Lancet **2**:499 (Sept. 3) 1921.

77. Barker, L. F.: Diagnostic Criteria in Encephalitis and Encephalomyelitis, Arch. Neurol. & Psychiat. **6**:173 (Aug.) 1921.

78. Bassoe, Peter: Diagnosis of Encephalitis, J. A. M. A. **79**:2223 (Dec. 30) 1922.

79. Price, G. E.: Encephalitis; Recurrence of Symptoms One and One-Half Years After Apparent Recovery, J. A. M. A. **78**:716 (March 11) 1922.

80. Blakeslee, G. A.: Neurol. Bull. **3**:159, 1921.

81. Duzar, J., and Baló, J.: Jahrb. f. Kinderh. **99**:209 (Sept.) 1922.

is also emphasized by Voigt[82] and others, and the prevalence of local and general convulsions causing difficulty in diagnosis is mentioned by Stadelmann.[83] A diagnostic aid was the fact that Pandy's reaction was almost always negative, though lymphocytosis existed frequently.

In twenty-eight cases analyzed by Moore[84] 80 per cent. of the patients were somnolent and 20 per cent. died. The rare occurrence of the disease in a new-born has been recorded by Hoobler.[85]

Kernig's and Brudzinski's signs, as noted by various writers, for example Bardach,[86] were missing even in meningeal irritation, this serving as a valuable differential diagnostic factor as regards tuberculous meningitis. The sketches given by Bardach of the symptomatology, as noted by her during the epidemic in Dusseldorf (1920 and in 1921), make the complexity of the clinical picture again apparent. Cases were seen with the picture of dementia praecox, glycosuria, striking relapses and marked intestinal contractions. Massari had described similar contractions of the ileum and cecum of such violent character that a surgical intra-abdominal affection was suspected and laparotomy performed; and in the three cases of epidemic encephalomyelitis reported by Bolaffio,[87] intense abdominal pains suggested appendicitis or ileus. The author adds that in similar cases operation has been performed, with negative findings after laparotomy.

Of the twenty-seven cases reported by Palitzsch[88] the majority represented the hypertonic akinetic type, frequently in combination with tremor, ocular paralysis and lethargy; the minority representing the atonic hyperkinetic form with muscular atonia, choreic or athetotic movements and myoclonia.

Purely spinal types are discussed by Riley.[89] Symptomatically, they are divided into two groups: (1) ventral poliomyelitis, with the irritative and paralytic subgroups; and (2) the transverse myelitic type. There are transitional forms.

Sequelae.—The greater our experience with the disease, the more are we impressed by the frequency and seriousness of its sequelae, which are so characteristic that they allow a retrospective diagnosis of the nature of the previous acute disease.

With the exception of one, the forty-five patients observed by Hofstadt[90] who were discharged from hospital as cured after the acute stage proved later not to be cured. After a free interval of from one to nine weeks, they manifested various morbid symptoms of a striking character, then new to the pediatrician. Among the polymorphous syndromes of the sequelae, five principal characteristic groups could be discerned: 1. Agrypnia, the most frequent and extremely intractable, extending over months, characterized by a postponement of falling asleep and often also by reduction of the total sleeping time per day, and accompanied frequently by excessive nocturnal hyperkinesis of a great variety of types. 2. The amyostatic syndromes. 3. Chronic chorea and chorea-athetosis, a syndrome considered a manifestation of the extrapyramidal system. 4. The psychic disturbances of various forms, graded from slight alterations of personality or psychic transformations to marked hypomanic conditions; from mild to severe degrees of dementia and ethical defects. Flight of ideas, marked lack of control, exaggerated euphoria, psychomotor hyperactivity, destructive tendencies, lack of power to cencentrate, quarrelsomeness, talkativeness were encountered. The conditions often reminded one of the psychoses of manic character (hypomania). In another group of children, the psychic transformations were of a depressive type or the features had a semblance of hysteria or neuropathia. 5. Adiposogenital complex.

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[82] Voigt, O.: Monatschr. f. Kinderh. **21**:156 (May) 1921.

[83] Stadelmann, E.: Monatschr. f. Kinderh. **19**:294, 1921.

[84] Moore, C. U.: Northwest Med. **20**:176 (July) 1921.

[85] Hoobler, Raymond: Arch. Pediat. **38**:461, 1921.

[86] Bardach, M.: Monatschr. f. Kinderh. **22**:475 (Dec.) 1922.

[87] Bolaffio, A.: Riv. crit. di clin. med., July 15, 1922, p. 232.

[88] Palitzsch, F.: Deutsch. Arch. f. klin. Med. **135**:115 (Jan.) 1921.

[89] Riley, H. A.: Spinal Forms of Encephalitis, Arch. Neurol. & Psychiat. **5**:408 (April) 1921.

[90] Hofstadt, F.: Ztschr. f. Kinderh. **29**:272 (June) 1921.

Agrypnia seems to be capable of improvement eventually, while the amyostatic complexes probably are irreparable and in the course of years lead to dementia and death.

About one fourth of the cases of Price[91] terminated fatally, and the remainder were left with persistent sequelae; and Grossman,[92] among ninety-two patients, adults and children, discovered in sixty-two a more or less progressive involvement of the central nervous system, with forty-two of them manifesting a parkinsonian syndrome and various psychic disturbances. In the experience of Barker[93] complete recovery was the exception, perhaps 75 per cent. of the cases exhibiting residual phenomena as hyperkinetic, hyperesthetic and paresthetic syndromes, autonomic disorders, disturbances of coordination, pupillary and ciliary disturbances, sialorrhea and a number of minor and major psychoses. A considerable number of children were rendered permanently deficient mentally.

The great frequency of parkinsonian residues observable in France during the last two years has been commented upon by Laignel-Lavastine.[94]

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[91] Price, G. E.: Am. J. M. Sc. **163**:871 (June) 1922.

[92] Grossman, M.: Sequels of Encephalitis, J. A. M. A. **78**:959 (April 1) 1922.

[93] Barker, L. F.: Sequels of Epidemic (Lethargic) Encephalitis and Their Treatment, J. A. M. A. **78**:1417 (May 6) 1922.

[94] Laignel-Lavastine: Médicine **3**:325 (Feb.) 1922.

It is especially the nocturnal wakefulness and diurnal somnolence, the inversion of the rhythm of sleep that forms the subject of numerous papers. Rolleston and Fletcher,[95] Progulski and Groebel,[96] Rutimeyer,[97] Reh,[98] Hofstadt,[99] Janecke,[100] Franconi,[101] Roasenda,[102] Zalla[103] and others have reported such serious sleep disturbances, often associated with delirious choreic states, restless agitation with singing, whistling, tossing from side to side, shouting and talking; partly also in association with changes of character and mind.

Parker[104] analyzes striking disorders of the respiratory rhythm, or constant dyspnea, Aronson[105] describes tachyrespiria, and Haas[106] describes attacks of forced breathing (hyperpnea) that invariably ended in the pseudotetany syndrome.

Precocious sexual feelings and intense eroticism were observed by Leahy and Sands.[107] Kirschbaum[108] reports asocial tendencies, brutality and moral insanity. Bonhoeffer[109] has similar experiences. Kauders[110] studying the large material of the Wagner Jauregg clinic at Vienna, saw repeatedly moria-like mental states with silly cheerfulness, desultory thinking, tendency to punning, euphoric dementia, intellectual defects and cases of extreme psychomotor restlessness, "hyperkinetic motility psychoses," and stereotyped movements. Similar experiences were met by Staehelin[111] in Zürich, Hohman,[112] Paterson and Spence,[113] and Cruchet.[114] Burt[115] gives a synopsis of the English publications on psychic sequelae, with the purpose of bringing this etiologic factor in antisocial behavior to the attention of those who deal with the criminality of children.

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95. Fletcher, H. M.: Brit. J. Dis. Child. **18**:69 (April-June) 1921.
96. Progulski, S., and Groebel, A.: München. med. Wchnschr. **68**:451 (April 15) 1921.
97. Rutimeyer, W.: Schweiz. med. Wchnschr. **51**:7 (Jan. 6) 1921.
98. Reh, T.: Rev. med. de la Suisse Rom. **41**:184 (March) 1921.
99. Hofstadt, F.: München. med. Wchnschr. **67**:1400 (Dec. 3) 1920.
100. Janecke, A.: Deutsch. med. Wchnschr. **46**:1388 (Dec. 9) 1920.
101. Franconi, C.: Policlinico **28**:575, 1921.
102. Roasenda: Policlinico **28**:181 (Feb. 17) 1921.
103. Zalla: Riv. di patol. nerv. **25**:375, 1920.
104. Parker, H. L.: Disturbances of Respiratory Rhythm in Children, Arch. Neurol. & Psychiat. **8**:630 (Dec.) 1922.
105. Aronson, L. S.: Neurol. Bull. **3**:113, 1921.
106. Haas, S. V.: Arch. Pediat. **38**:785, 1921.
107. Leahy, S. R., and Sands, I. J.: Mental Disorders in Children Following Encephalitis, J. A. M. A. **76**:373 (Feb. 5) 1921.
108. Kirschbaum, M.: Ztschr. f. ges. Neurol. u. Psychiat. **73**:599, 1921.
109. Bonhoeffer, K.: Klin. Wchnschr. **1**:1446 (July 15) 1922.
110. Kauders: Ztschr. f. ges. Neurol. u. Psychiat. **74**:431, 1922.
111. Staehelin, J. E.: Ztschr. f. ges. Neurol. u. Psychiat. **77**:171, 1922.
112. Hohman, L. B.: Bull. Johns Hopkins Hosp. **33**:372 (Oct.) 1922.
113. Paterson, D., and Spence, J. C.: Lancet **2**:491 (Sept. 3) 1921.
114. Cruchet, R.: J. de méd. de Bordeaux **92**:20 (Jan.) 1921.
115. Burt, C.: Brit. J. Psychol. **2**:237 (April) 1922.

Duverger and Barré[116] state that various ocular manifestations must be anticipated for years to come and should not be mistaken for neurosyphilis.

Among the rare consequences of epidemic encephalitis, hypophysial syndromes with adiposity and genital atrophy are reported by Stiefler,[117] Kauders,[110] Mayer,[118] Bychowski,[119] Bertolani,[120] Barkman[121] and others; obesity, by Livet;[122] myasthenia gravis and progressive lipodystrophy, by Sarbó;[123] pubertas praecox by Stern;[124] a very oily seborrhea of the face (Salbengesicht) by Stiefler[125] in an adult.

Spinal Fluid.—The conditions of the spinal fluid have been described at length by Kraus and Pardee[126] and Eskuchen.[127] The latter, summarizing the available data, states that two spinal fluid syndromes are to a certain degree characteristic: (1) pleocytosis, globulin increase, "luetic" gold curve and hyperglycorrhachia; (2) the triad: cytoglobulin dissociation (high cell count in proportion to the amount of globulin) "luetic" gold curve and hyperglycorrhachia. Other contributions were made by Thalhimer[128] and Foster[129] on hyperglycorrhachia; by Howell,[130] Davis and Kraus,[131] Happ and Mason,[132] on the colloidal gold reaction. The presence of an antibody was demonstrated by Quest[133] by means of intradermal autoseroreaction.

Pathologic Anatomy.—The histopathologic studies by Siegmund[134] in twenty-one cases revealed the typical pictures, characterized by perivascular round and plasma cell infiltration, nodular or diffuse proliferation of glia cells, degenerative processes in the ganglion cells and neuronophagia. The site of predilection is the gray matter around the aquaeductus, the third ventricle and the lateral ventricles, without sparing entirely, however, other parts of the brain, including the white matter. In seven cases, there were meningitic changes; in three cases the spinal cord was involved; and in six cases, a streptococcus was isolated. Pathologically and anatomically, the affection is classified by the author in the group of poliomyelitis, typhus fever and trypanosomiasis (sleeping-sickness).

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[116] Duverger and Barré: Bull. méd., Paris, 1921, p. 361.

[117] Stiefler: Monatschr. f. Psych. u. Neurol., August, 1921.

[118] Mayer, W.: München. med. Wchnschr. **68**:552 (May 6) 1921.

[119] Bychowski, Z.: Ztschr. f. ges. Neurol. u. Psychiat. **76**:508, 1922.

[120] Bertolani: Riv. sper. de freniat. **45**:467, 1922.

[121] Barkman, A.: Acta med. Scandinav. **56**:188 (March) 1922.

[122] Livet, L.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:656 (May 6) 1921.

[123] Sarbó: Orvosi hetil. **65**, 1921; Deutsch. Ztschr. f. Neurol. **74**:285, 1922.

[124] Stern, F.: Med. klin. **18**:864 (July 2) 1922.

[125] Stiefler: Ztschr. f. Neurol. u. Psychiat. **73**:455, 1921.

[126] Kraus, W. M., and Pardee, I. H.: Serology of Spinal Fluid and Blood in Encephalitis, Arch. Neurol. & Psychiat. **5**:710 (June) 1921.

[127] Eskuchen, K.: Ztschr. f. ges. Neurol. u. Psychiat. **76**:568, 1922.

[128] Thalhimer, William, and Updegraff, Helen: Sugar Content of Blood and Spinal Fluid in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **8**:15 (July) 1922.

[129] Foster, H. E.: Hyperglycorachia in Encephalitis, J. A. M. A. **76**:1300 (May 7) 1921.

[130] Howell, K. M.: Colloidal Gold Curve in Encephalitis, Arch. Neurol. & Psychiat. **7**:229 (Feb.) 1922.

[131] Davis, T. K., and Kraus, W. M.: Am. J. M. Sc. **161**:109 (Jan.) 1921.

[132] Happ, W. M., and Mason, V. R.: Bull. Johns Hopkins Hosp. **32**:137 (May) 1921.

[133] Quest, R.: Jahrb. f. Kinderh. **96**:324, 1921.

[134] Siegmund, H.: Frankfurt. Ztschr. f. Pathol. **25**:526, 1921.

Minute pathologic findings are recorded by Grütter.[135] Da Fano[136] writes on the histopathology, and Lucksch,[137] on ganglion cells. The findings in a case of epidemic encephalitis with myelitis are detailed by Spiller.[138] Calcification of cerebral vessels is described by Dürck,[139] and the subject of disturbances of the liver in epidemic encephalitis is taken up by Stern and Meyer-Bisch.[140] Duzar and Balo[81] describe briefly the pathologic and histologic findings in seven infants.

Epidemiology, Etiology and Bacteriology.—An increasing number of publications speak in favor of the contagious nature of the disease. Kling,[141] who under the most favorable conditions studied the manner of propagation of the disease in a sparsely populated part of Lapland, could follow up direct transmissions from person to person. The incubation time was ten days, and the virus was demonstrated in the nasopharynx of well persons who had been in contact with the sick. Very frequent were the abortive cases with catarrhal symptoms predominating. Convincing evidences of contagiosity are farther recorded by Netter,[142] Stiefler,[143] Claude and de Laulerie,[144] Roger and Blanchard[145] and Pecori.[146] Placental transmission is reported by Mercier.[147] Investigations of the filtrable virus were carried on by

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[135] Grütter, E.: Ztschr. f. ges. Neurol. u. Psychiat. **72**:29, 1921.

[136] Da Fano, C.: Brit. M. J. **1**:153 (Jan. 29) 1921.

[137] Lucksch: Klin. Wchnschr. **1**:1528, 1922.

[138] Spiller, W. G.: Encephalitis with Myelitis, Arch. Neurol. & Psychiat. **7**:739 (June) 1922.

[139] Dürck, H.: Ztschr. f. ges. Neurol. u. Psychiat. **72**:179, 1921.

[140] Stern, F., and Meyer-Bisch, R.: Klin. Wchnschr. **1**:1559 (July 29) 1922.

[141] Kling: Norsk Mag. f. Lævidensk. **83**:843, 1922; Current Comment, J. A. M. A. **79**:1771 (Nov. 13) 1922.

[142] Netter et al.: Bull. Acad. de méd. **85**:278 (March 8) 1921.

[143] Stiefler: Ztschr. f. ges. Neurol. u. Psychiat. **74**:396, 1922.

[144] Claude, H., and de Laulerie, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:36 (Jan. 21) 1921.

[145] Roger, H., and Blanchard, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:40 (Jan. 21) 1921.

[146] Pecori: Ann. d'ig. sper. **31**:32, 1921.

[147] Mercier, R. et al.: Bull. Acad. de med. **85**:625 (May 31) 1921.

Netter, Césari and Durand,[148] Thalhimer,[149] Davide and Liljenquist,[150] Bastei,[151] Levaditi and Harvier [152] and others.

Economo [153] holds *Diplostreptococcus pleomorphus* of Wiesner (1917) as the causative agent, and he cites Gross and Reichhard of Heidelberg, who found this micro-organism in all their cases of epidemic encephalitis.

Rosenow [154] isolated a streptococcus of the green producing variety in a case of encephalitis, and also proved the infectious nature of epidemic [155] hiccup. His experimental results suggest a relationship between epidemic hiccup and encephalitis.

That epidemic encephalitis and poliomyelitis can be distinguished by the power of blood serum of patients convalescent from poliomyelitis to neutralize the virus of poliomyelitis, the serum of those convalescent from encephalitis being void of this power, has been demonstrated by the immunologic studies of Amoss.[156]

The finding by Hilgermann, Lauxen and C. Shaw [157] of parasites in the blood during a recurrence demonstrates that the disease may last a long time, the persistence of the parasite within the human body involving a permanent danger of propagation.

Treatment.—In the experience of Economo [153] the use of hexamethylenamin and injections of Pregl's iodin solution in large doses had striking results. Dattner [158] used successfully injections of Pregl's solution and an iodin preparation with typhoid vaccine. Helmholz and Rosenow [159] obtained striking results in three patients treated with serum from a horse repeatedly injected with streptococcus that had been isolated in a patient with typical encephalitis. Piticariu [160] used suc-

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148. Netter, A.; Césari and Durand, H.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:751 (May 13) 1921.

149. Thalhimer, William: Encephalitis Cultural and Experimental Studies, Arch. Neurol & Psychiat. **5**:113 (Feb.) 1921.

150. Kling, C.; Davide, H., and Liljenquist, F.: Hygiea **83**:566 (Sept. 16) 1921; abstr., J. A. M. A. **77**:1613 (Nov. 13) 1921.

151. Bastei, P.: Arch. per le sc. med., Torino **44**:212, 1921.

152. Levaditi, C., and Harvier, P.: Compt. rend. Soc. de biol. **84**:300, 957, 1921; Ann. de l'Inst. Pasteur, 1922. Harvier, P.: Paris méd. **11**:485, 1921; abstr. J. A. M. A. **77**:495 (Aug. 6) 1921.

153. Economo: Wien. med. Wchnschr. **71**:1322, 1921.

154. Rosenow, E. C.: Etiology of Encephalitis, J. A. M. A. **79**:443 (Aug. 5) 1922.

155. Rosenow, E. C.: Diaphragmatic Spasms in Animals Produced with a Streptococcus from Epidemic Hiccup, J. A. M. A. **76**:1745 (June 18) 1921; Northwest Med. **21**:329 (Sept.) 1922.

156. Amoss, H. L.: J. Exper. Med. **33**:187 (Feb.) 1921.

157. Hilgermann, Lauxen, and Shaw, C.: Med. Klin. **18**:17 (Jan. 1) 1922.

158. Dattner, B.: Wien. klin. Wchnschr. **34**:351, 1921.

159. Helmholz, H. F., and Rosenow, E. C.: Encephalitis Treated with Specific Serum, J. A. M. A. **79**:2068 (Dec. 16) 1922.

160. Piticariu, I.: Wien. klin. Wchnschr. **35**:441 (May 11) 1922.

cessfully intravenous injections of the patient's own lumbar puncture fluid, which, he believes, may contain antibodies. Voigt[82] saw in two cases a striking subsidence of the symptoms regularly following repeated lumbar punctures, until recovery took place. Leahy and Sands[161] write on the management of children presenting postencephalitic syndromes, such as the reversal from nocturnal to diurnal sleep. Laignel-Lavastine,[94] Barré and Reys[162] and Radovici and Nicolesco[163] report some results from scopolamin and atropin in involuntary movements and in the parkinsonian syndrome. Cheinisse,[164] who reviews the different publications on treatment, asserts that none have stood the test of time except the turpentine fixation abscess, which reduces the mortality considerably.

The following contributions, though not exclusively dealing with the disease in childhood, are of interest for the pediatrician: the article of Hunt[165] on striatal and thalamic types; of Abrahamson[166] on motor disturbances; of Kirby and Davis;[167] of Jones and Raphael[168] on the psychiatric features of the disease; of Grossman[169] on late results; of Pearl[170] on statistical notes; of Alexander[171] on treatment; the Public Health Report[172] on world wide prevalence; of Kahlmeter,[173] Reeves,[174] Happ and Mason[175] on clinical studies; Mayer[176] on late conditions; Isserlin[177] on extrapyramidal disorders after encephalitis; of Mingazzini,[178] von Monakow[179] on morphology and pathogenesis, and a French committee report[180] on the history of the disease.

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161. Leahy, S. R., and Sands, C. J.: New York M. J. **114**:166 (Aug. 3) 1921.

162. Barré, J. A., and Reys, L.: Paris méd. **11**:261 (Oct. 1) 1921; Bull. méd., Paris **35**:351 (April) 1921.

163. Radovici, A., and Nicolesco, J. F.: Presse méd. **29**:83 (Jan. 29) 1921.

164. Cheinisse, L.: Presse méd. **29**:146 (Feb. 19) 1921; abstr., J. A. M. A. **76**:967 (April 2) 1921.

165. Hunt, J. R.: Am. J. M. Sc. **162**:481 (Oct.) 1921.

166. Abrahamson, I.: Motor Disturbances in Encephalitis, Arch. Neurol. & Psychiat. **5**:33 (Jan.) 1921.

167. Kirby, G. H., and Davis, T. K.: Psychiatric Aspects of Epidemic Encephalitis, Arch. Neurol. & Psychiat. **5**:491 (May) 1921.

168. Jones, B. L., and Raphael, T.: Psychiatric Features of So-Called Encephalitis, Arch. Neurol. & Psychiat. **5**:150 (Feb.) 1921.

169. Grossman, M.: Late Results in Encephalitis, Arch. Neurol. & Psychiat. **5**:580 (May 1921.

170. Pearl, R.: Bull. Johns Hopkins Hosp. **32**:221 (July) 1921.

171. Alexander, A.: Deutsch. med. Wchnschr. **47**:1547, 1921.

172. Public Health Report **36**:602, 1921.

173. Kahlmeter, G.: Clinical Aspects of Encephalitis, München. med. Wchnschr. **68**:669 (June 3) 1921.

174. Reeves, R. S.: New York M. J. **114**:702 (Dec. 21) 1921.

175. Happ, W. M., and Mason, V. R.: Bull. Johns Hopkins Hosp. **32**:137 (May) 1921.

176. Mayer, W.: München. med. Wchnschr. **69**:552 (May 6) 1921.

177. Isserlin, A.: Deutsch. Ztschr. f. Nervenh. **74**:319, 1922.

178. Mingazzini, G.: Zentralbl. f. ges. Neurol. u. Psychiat. **63**:199, 1921.

179. Von Monakow, C.: Schweiz. Arch. f. Neurol. u. Psychiat. **10**:3, 1922; abstr. Arch. Neurol. & Psychiat. **8**:299 (Sept.) 1922.

180. Bull. Acad. de méd. **85**:278, 1921.

CHOREA MINOR

The analysis of the chorea material at the Children's Hospital of Stockholm by Nordgren[181] established farther evidences for the rheumatic etiology of the disease in the demonstration of an increased seasonal incidence of chorea minor together with that of true rheumatic affections, and in the fact that among the 393 children with chorea, 193 had definite rheumatic histories. Pfaundler,[182] who in his abundant material never encountered chorea and rheumatic affections simultaneously as would be expected according to our pathogenetic conception, speaks of "successive syntropism" of these two diseases.

The necropsy findings by Schroeder[183] of endocarditis and pericarditis with typical Aschoff's nodular cells in the heart muscle of a 20 months old girl who suffered from chorea minor demonstrates again the relationship of the cerebral symptoms and rheumatic infection. The connection between chorea and focal infection became evident also in Yerger's[184] patient, who was promptly cured by adenectomy, the adenoids containing a suppurative sinus (Thornwaldt's disease). Berger[185] noted eosinophilia, averaging 7.6 per cent., with the maximum 26 per cent.

The differential diagnostic significance of Gordon's modified patellary reflex in chorea minor has been tested by Noeggerath[186] in sixty-eight schoolchildren without any indication of chorea, rheumatism or heart lesions. He found in seven children typical, and in several others a less marked, modified Gordon's reflex.

In a series of eighty-eight cases of Sydenham's chorea observed by Hammes[187] definite symptoms of a psychosis existed in about 20 per cent. No uniformity in the mental pictures was noted except that frequently distressing hallucinations were present, conforming to those observed in other toxic psychoses. The mental improvement was followed by rapid and complete recovery. F. R. Fry's remark that chorea is a form of encephalitis or encephalic reaction, the choreic psychoses being a partial manifestation thereof, is supported by the brain sections made by Greenfield and Wolfsohn[188] that presented a pathology very similar to that in lethargic encephalitis in the early stage; and by the necropsy findings of Gennaro Fiore[189] in two cases, consisting in a disseminated perivascular edematous alveolar encephalitis, most pronounced in the optic thalamus, the corpus striatum and the motor zone of the cortex.

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[181] Nordgren, R.: Acta pædiat. **2**:159, 1922.

[182] Pfaundler: Ztschr. f. Kinderh. **30**:100, 274, 1921.

[183] Schroeder, L. C.: Observations on the Etiology and Pathology of Chorea Minor, J. A. M. A. **79**:181 (July 15) 1922.

[184] Yerger, C. F.: Thronwaldt's Disease and Chorea, J. A. M. A. **76**:166 (Jan. 15) 1921.

[185] Berger, H. C.: Eosinophilia Occurring in Chorea, Am. J. Dis. Child. **21**:477 (May) 1921.

[186] Noeggerath, C.: Monatschr. f. Kinderh. **22**:657 (Feb.) 1922.

[187] Hammes, E. M.: Psychoses Associated with Sydenham's Chorea, J. A. M. A. **79**:804 (Sept. 2) 1922.

[188] Greenfield, J. G., and Wolfsohn, J. M.: Lancet **2**:603 (Sept. 16) 1922

While most authors urge rest and even isolation as one of the prime factors in the management of the disease, Irving[190] attaches great importance to recreation in the country or sea shore, with mild physical activities in the convalescent stage, under trained supervision. Well graded quiet games, etc., resulted in remarkable benefit to 123 choreic children.

Special active movements on a principle similar to that of Frenkel's exercise treatment proved successful in the experience of Krager.[191] Paulian and Dragesco[192] report good therapeutic results from intravenous or intraspinal injections of magnesium sulphate, and Bilotta[193] from intravenous injections of arsphenamin.

TUMORS OF THE BRAIN

Bartlett and Wollstein[194] state that among 4,563 necropsies at the Babies' Hospital, New York, there were nine cases of neoplasms of the brain (0.2 per cent.), the ages of the children ranging from 2 weeks to 3 years. Two neoplasms were located in the cerebrum and five in the cerebellum. All the latter were gliomas of the astrocytoma type. The supratentorial tumors existed in infants; one was a glioma, the other a congenital gliosarcoma. In the infants, the tumors had grown to a considerable size before they gave symptoms, which is explained by the distensibility of the skull and marked adaptability of the young brain to pressure applied gradually.

Convulsive phenomena in tumors of the posterior fossa are rare. Only nine among the forty-five cases studied by MacRobert and Feinier[195] had spasms arising from pressure in the cerebellum. Irregularity and sustained tonicity of the movements are the distinguishing features in comparison with the rhythmic clonic movements of the spasms arising in the forebrain. Forced movements, ticlike spasms in cranial nerves and respiratory embarrassment may develop.

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189. Fiore, Gennaro: Rev. de clin. pediat. **20**:193, 1922.
190. Irving, G. R.: Arch. Pediat. **39**:159 (March) 1922.
191. Krager, R.: Jahrb. f. Kinderh. **95**:261, 1921.
192. Paulian, O. E., and Dragesco, R.: Presse méd. **30**:680 (Aug. 9) 1922.
193. Bilotta, V.: Policlinico (sez. prat.) **28**:545 (April 18) 1921.
194. Bartlett, F. H., and Wollstein, Martha: Arch. Pediat. **39**:386, 1922.
195. MacRobert, R. G., and Feinier, L.: Cerebellar Fits, Arch. Neurol. & Psychiat. **5**:296 (March) 1921.

A paper of paramount interest and based on a wide experience has been written by Dandy [196] on treatment of brain tumors. The author insists that treatment must be based on early and precise localization of the tumor and consist in the complete operative removal. The tumor can be diagnosed and located with accuracy or eliminated by cerebral pneumography. In more than 200 injections, the author never failed to make an accurate localization or to find the tumor at operation.

Menninger [197] testifies to the great value of Dandy's method, but points out certain diagnostic limitations. A number of by-effects of intraspinal insufflation were described by Wideröe.[198] A diagnostically instructive case of the syndrome of the occipitocerebellovertebral angle has been described by Nobécourt and Paraf [199] in a boy who had paralysis of the outer branch of the spinal nerve that innervates the neck musculature, atrophy and subsultus tendinum on the right side, with anesthesia in the area of the right second occipital nerve and slight cerebellar symptoms. Extirpation of the tuberculous tumor at the angle resulted in cure.

Two examples of intracranial dermoid cysts were presented by Horrax [200]; and a case of echinococcus cyst the size of two fists in a boy of 8, filling out the ventricles, by Dévé.[201]

Brain Abscess.—A case of cerebellar diplococcus abscess following mastoiditis, with successful operation for both conditions, is cited by McCoy.[202] The interesting feature was that lethargic encephalitis complicated the clinical picture after the second (cerebellar) operation. Complete recovery ensued.

INFANTILE CEREBRAL PARALYSIS

A unique case of Little's disease in a baby born nonasphyctic by Cesarean section in a case of contracted pelvis has been reported by Tauber.[203] The brain hemorrhage was charged to pressure of the symphysis on the skull during the expulsion period or to overriding of the cranial bones.

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196. Dandy, W. E.: Treatment of Brain Tumors, J. A. M. A. **77**:1853 (Dec. 10) 1921.

197. Menninger, K. A.: Dandy Method of Localizing Brain Tumors by Roentgen Ray, Arch. Neurol. & Psychiat. **5**:438 (April) 1921.

198. Wideröe, S.: Norsk Mag. f. Lægevidensk. **82**:491 (July) 1921.

199. Nobécourt, P., and Paraf, J.: Bull. Soc. de pediat. **20**:327, 1922.

200. Horrax, Gilbert: Dermal Versus Epidermal Cholesteatomas Having Their Attachment in Cerebral Envelops, Arch. Neurol. & Psychiat. **8**:265 (Sept.) 1922.

201. Dévé: Compt. rend. Soc. de biol. **86**:1062, 1922.

202. McCoy, John: Case of Cerebellar Abscess with Very Unusual Features; Operations; Recovery, J. A. M. A. **77**:1333 (Oct. 22) 1921.

203. Tauber: Wien. klin. Wchnschr. **35**:499 (June 1) 1922.

The atonic cerebellar type of diplegia was the subject of a paper by Hempelmann,[204] who reports two cases. In one of them there was distinct asymmetry between the cerebral hemispheres and the two lobes of the cerebellum, due to development defects.

The motor disturbances in infantile encephalopathias of children are classified by Babonneix [205] into various groups. The changes of tonus may be contractures of pyramidal origin, rigidity of pallidal origin and decerebrate rigidity, which possibly originates in the nucleus ruber. The psychomotor disturbances are chiefly paralysis of hemiplegic, paraplegic or localized character. They may be complicated by cerebral syndromes, namely by convulsions, involuntary movements such as athetosis, chorea and synkinesis; by intellectual disorders, hypertonia, awkwardness (paratonia) and also by cerebellar symptoms.

The rarity of hemianopsia in infantile cerebral hemiplegia induced Babonneix and Hallez [206] to report this condition in a child 22 months old.

The end-results of Stoffel operation in seven cases of spastic paralysis, improvement in comfort and appearance of the patient, have been demonstrated before the Philadelphia Pediatric Society by Gill.[207]

Manifestations of infantile pseudobulbar paralysis existed in 2.83 per cent. of 600 applicants for treatment at the University dispensary for speech and voice disturbances at the Berlin Charité. The principal symptoms of the affection, described by Fiebig,[208] were dysarthria, stuttering and jerky pronunciation. The speech was nasal owing to paresis of the soft palate. There was dribbling of saliva, choking and regurgitation of fluids through the nose, with affection of the deglutition muscles. As the focus is in the cortex and not in the oblongata, there is no atrophy or degeneration reaction of the muscles. Other muscular functions which require fine coordination were often disturbed, such as sewing, embroidering, drawing, climbing stairs, etc. Though the patients are frequently mistaken for imbecile, they are by no means intellectually defective. There is a tendency to improvement in the course of years, especially with proper exercise and speech training. A number of interesting examples illustrate the clinical pictures and diagnostic features of the affection.

The complete decerebrate rigidity, observed by Thomson and Piney,[209] in an infant 4 months old had its pathologico-anatomic basis in

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204. Hempelmann, T. C.: Arch. Pediat. **39**:411, 1922.
205. Babonneix: J. de méd. de Paris **41**:307, 1922.
206. Babonneix, L., and Hallez, G. L.: Gaz. d. hôp. **95**:997, 1922.
207. Gill, A. B.: Arch. Pediat. **39**:320 (May) 1922.
208. Fiebig, M.: Arch. f. Kinderh. **6**:425 (Feb.) 1921
209. Thomson, A. P., and Piney, A.: Lancet **2**:1105 (Nov. 26) 1921.

extreme softening of the large areas of the cortex, with an almost complete destruction of the deeper layers of the cortex and adjacent white matter and endarteritis obliterans in many vessels.

Wachendorf[210] recalls that the prospects of improvement of paralyses and choreiform and athetoid movements in cerebral infantile paralysis, from operations are unfortunately small. Epilepsy from birth trauma, on the other hand, should be treated early, on the same principle as traumatic epilepsy in general by elimination of scars, cysts, adhesions and removal of bone fragments. The cases of traumatic and jacksonian epilepsy, according to Tilmann, show 18 per cent. of cures. Operations in two of Wachendorf's cases were followed by improvement; in one case, by death in status epilepticus.

BASAL GANGLIONS

Of great interest for the pediatrician is the elaborate and instructive treatise issued by Prof. O. Foerster[211] of Breslau, who, basing his work on a very abundant material, gives an analysis of the physiopathology of striate motor disturbances. He discusses the various forms of Little's disease, dystonia lordotica, myoclonia, certain tics, spastic torticollis and other motor disorders which especially after our great experience derived from epidemic encephalitis have to be connected with the corpus striatum. The destructive pathologic process in Voigt's status marmoratus and possibly in status dysmyelinisatus of the globus pallidus is congenital. A hereditary factor exists in Huntington's chorea, and pseudosclerosis. The etiology of Wilson's disease and of tuberous sclerosis with its occasional striate symptoms is unknown. Other groups of corpus striatum affections are contusions, hemorrhages, as in infantile cerebral paralysis and vascular changes; poisoning with lighting gas, carbon monoxid and possibly manganese; tumors, hydrocephalus and inflammatory processes, as in congenital syphilis and especially in epidemic encephalitis. The author saw generalized athetosis follow epidemic meningitis. Chorea minor is generally admitted to be an infectious brain disease with localizations in the cortex, basal ganglions, nucleus dentatus (Alzheimer) and crura cerebelli. The hypokinetic pallidum syndrome comprises inconstant tremor, increased plastic muscular tone, anomalies of attitude of body and position of extremities, adaptation with fixation rigidity, and catalepsy of limbs. There is a paucity of reactive and expressive movements, slowness, reduced excursion and persistence of voluntary movements and absence of associative movements.

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210. Wachendorf, K.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **34**:64, 1921.

211. Foerster, O.: Ztschr. f. ges. Neurol. u. Psychiat. **73**:1-169, 1921.

The athetotic striatum syndrome, originating in the nucleus caudatus and putamen, comprises athetotic movements at rest, reduction of the plastic muscle tone during the intervals, and anomalies in attitude of trunk and extremities; overextensibility of muscles and a tendency to fixation rigidity. There exist also extensive reactive, expressive and associative movements, which may cause inability to sit and walk.

The components of the choreic syndrome are choreic movements during rest; lessening of the plastic muscle tone; lessening of resistance to stretching and overextensibility of muscles; transitory fixation rigidity, intense reactive and expressive and associative movements during the execution of voluntary movements; inability to sit, stand and walk in severe cases, and replacement of these functions by "massive reactive movements" of the whole body, of choreic character.

One hundred and seventy-three illustrations, including many in children, give a conception of the various motor disorders, demonstrating strikingly extreme distortions of body and limbs in universal and localized forms, compulsory laughing, grimaces, centaur-attitudes of body, torticollis, etc. An elaborate review of the entire subject is given by Crothers,[212] by Bickel [213] and Stertz [214] and others. The first author relates six illustrative observations of his own.

There can be no doubt that among the cerebral disturbances in infants striatal signs may be present ascribable to injury of vessels in the corpus striatum in connection with difficult birth. Babonneix [215] remarks that these lesions may arrest farther development and be followed by persisting conditions.

Although occurring usually in children of the Jewish race, dystonia musculorum progressiva is not confined to that race. Flater [216] reports the disease in a 10 year old gentile girl. In the case of Howe [217] the mother only was of Jewish blood. Another interesting feature in the latter case was that the first disturbances were in the trunk, with shrugging of the shoulders, and a quavering voice, the speech becoming unintelligible within six months. The condition persisted three years and then improved.

Jacob [218] describes typical torsion dystonia in a 14 year old Jewish boy, whose younger brother suffered from symptoms of lenticular character. In a second case, a 12½ year old gentile boy, whose condition was at first diagnosed as torsion dystonia, developed later a clinical picture of pseudosclerosis, with changes in the liver.

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[212] Crothers, B.: Lesions of Corpus Striatum in Childhood, Am. J. Dis. Child. **22**:145 (Aug.) 1921.

[213] Bickel, G.: Rev. med. de la Suisse Rom. **42**:365, 1922.

[214] Stertz, G.: Beihefte z. Monatschr. f. Psychiat. u. Neurol., 1921, pp. 1-96.

[215] Babonneix: Ann. de méd. **12**:70 (July) 1922; abstr. J. A. M. A. **79**:1178 (Sept. 30) 1922.

[216] Flater, Adolf: Ztschr. f. ges. Neurol. u. Psychiat. **69**:27, 1921.

[217] Howe, H.: Neurol. Bull. **3**:253 (July) 1921.

[218] Jacob, Charlotte: Arch. f. Psychiat. u. Nervenkrankh. **65**:540, 1922.

Attention should be given to the existence of a myostatic or postural variant of this disease and to the association with fragmentary and almost complete decerebrate rigidity, which has been studied by Wechsler and Brock[219] in six hitherto unreported cases of dystonia musculorum deformans with atypical features.

A study of the types of extrapyramidal rigidity and extrapyramidal pseudobulbar paralysis (akinetic hypertonic bulbar syndrome) in connection with lethargic encephalitis has been contributed by Gerstmann and Schilder[220] of the neurologic clinic at Vienna.

The Magnus and DeKlein phenomenon, a phenomenon of decerebration like decerebrate rigidity, has been analyzed by Meyers[221] in two cases of spastic paralysis, in which the patients presented spontaneous decerebrate attitudes and both types of the cervical reaction. The one child was unable to remain on the back, turning invariably to the left side around onto the abdomen. This condition is referred to generalized atrophy of the cerebellum found postmortem, the left hemisphere being much smaller than the right. The symptoms common to both children are explained by a congenital affection of the lenticular zone, established by Hassin. The author offers a new theory in the physiologic interpretation of the decerebrate attitudes.

Goodhart[222] alone and in company with Tilney[223] studied various postencephalitic deformities of motion by means of film-reels. The motions slowed down served as a basis for what these authors term bradykinetic analysis.

SCLEROSIS

Multiple sclerosis occurs in all ages. It has been described in about a hundred instances in children, occurring even at the early age of 1½, 3 and 4 years. Wechsler[224] adds four cases from his own records, one beginning at 6½, one at 8 and two at 14 years of age. A histopathologic study of acute multiple sclerosis in a girl of 4½ has been published by Neubürger.[225]

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219. Wechsler, J. S., and Brock, S.: Dystonia Musculorum Deformans, Arch. Neurol. & Psychiat. **8**:538 (Nov.) 1922.

220. Gerstmann, J., and Schilder, P.: Ztschr. f. ges. Neurol. u. Psychiat. **70**:35, 1921.

221. Meyers, I. L.: Magnus and DeKlein Phenomena in Brain Lesions of Man, Arch. Neurol. & Psychiat. **8**:383 (Oct.) 1922.

222. Goodhart, S. P.: Postencephalitis Deformities of Motion, Arch. Neurol. & Psychiat. **8**:652 (Dec.) 1922.

223. Goodhart, S. P., and Tilney, F.: Neurol. Bull. **3**:295 (Sept.-Oct.) 1922.

224. Wechsler, I. S.: Statistics of Multiple Sclerosis, Arch. Neurol. & Psychiat. **8**:59 (July) 1922.

225. Neubürger, K.: Ztschr. f. ges. Neurol. u. Psychiat. **76**:384, 1922.

TUBEROUS SCLEROSIS

Freeman,[226] after a review of the literature on tuberous sclerosis, reports his observations in a 6 year old child, giving the necropsy record and the results of the microscopic examination in great detail.

As six cases of this affection presented findings of tumor formations of the papilla optica and retina, Hoeve [227] concludes that such tumors may belong to the syndrome of the disease.

The association of tuberous sclerosis with pubertas praecox is recorded by Krabbe,[228] who holds the view that both conditions are due to one basic factor, a constitutional disturbance in the equilibrium of tissues.

The typical triad of hypernephroma, tuberous sclerosis and adenoma sebaceum in a boy of 10 has been reported by Hyman.[229] The patient had convulsions, marked mental defects and athetosis. Innumerable nodular eruptions on the face and a tumor of the right kidney led to the clinical diagnosis. Nephrectomy revealed hypernephroma.

Diffuse Cerebral Sclerosis (Strümpell's Disease).—The discovery by Giannuli [230] of numerous spirochetes in diffuse brain sclerosis (Strümpell's disease), which were arranged in nests in the cortex, being possibly degeneration forms of *Spirocheta pallida* makes it appear that the affection is a chronic interstitial encephalitis, and that in its pathogenesis not only endogenous but also exogenous elements—*Spirochaeta pallida*—may play a rôle.

SPINAL CORD

An interesting case of permanent disturbance of temperature due to birth trauma of the cervical cord and exemplifying the failure of thermoregulation as in experimental destruction of the cervical cord in animals is cited by Feer.[231] The boy, who was born with a foot presenting, had, in addition to certain signs of a spinal lesion of the cervical region, abnormal temperatures throughout his life with great changes, depending on external conditions, rising, according to circumstances, to or above 41 degrees (Celsius) or dropping to 36 or 35.5. Death ensued on the two hundred and twenty-sixth day. The postmortem examination verified the existence of cord injury from the sixth to the seventh cervical segment.

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226. Freeman, W.: Tuberous Sclerosis, Arch. Neurol. & Psychiat. **8**:614 (Dec.) 1922.

227. Hoeve, J.: Graefes Arch, f. Ophth. **105**:880, 1921.

228. Krabbe, K. H.: Encéphale **17**:281, 437, 496, 1922.

229. Hyman, A.: J. Urol. **8**:317 (Oct.) 1922.

230. Giannuli: Deutsch. Ztschr. f. Nervenh. **71**:306, 1921; Riv. sper. freniat. **44**:287, 1920.

231. Feer, E.: Tag. d. Deutsch. ges. f. Kinderh., 1921; Monatschr. f. Kinderheilk. **22**:203, 1921.

Powers[232] collected seven cases of postdiphtheritic disseminated myelitis or sclerosis and adds one instance of his own, in a boy of 10. The clinical picture was complete but did not terminate in the sclerotic stage, complete recovery ensuing.

Classic syringomyelia, a very rare affection in childhood, is described by De Villaverde[233] in a girl of 15. Parker[234] gives a comprehensive summary of the literature on juvenile tabes and reports seven of his own observations. In all, Westphal's sign was present; in six, diminished sensibility; in four, the pupils were immobile (large); in three cases, Argyll Robertson pupils, optic atrophy, crises, lightning pains, incoordination and hypotonia were present; in two cases, there was incontinence of urine; in one, ataxia. In three patients, the spinal fluid findings, strange to say, were negative. The cases agree well with those of other authors in regard to the paucity of physical signs, the long insidious course and the rarity of ataxia and other features that render juvenile tabes distinct from the adult form.

The view expressed by a number of authors that, in addition to syphilis, as generally recognized, an inherited predisposition, a constitutional inferiority of the nervous system must be assumed as a cooperative factor in juvenile tabes, has found strong support from the studies by Baumgarten[235] of 130 cases gathered from the literature. In 59.38 per cent. of cases with exact anamnesis, metasyphilitic affections, such as tabes or paresis, existed in one or in both parents.

Rosenheck[236] reports typical tabes juvenalis, with pupillary inequality, at the age of 12, as the first sign, subjective disturbances appearing three years later.

An important contribution to neurology was again made by the work of Ayer[237] on cistern puncture and arachnoid block. He worked out a method of combined cistern and lumbar puncture for the determination of subarachnoid block, especially with reference to the early diagnosis of cord tumors.

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[232] Powers, H.: Boston M. & S. J. **186**:45 (Jan. 12) 1922.

[233] De Villaverde, J. M.: Arch. españ. de pediat. **5**:321 (June) 1921.

[234] Parker, H. L.: Juvenile Tabes, Arch. Neurol. & Psychiat. **5**:121 (Feb.) 1921.

[235] Baumgarten, C.: Ztschr. f. ges. Neurol. u. Psychiat. **71**:321, 1922.

[236] Rosenheck, C.: Juvenile Tabes, J. A. M. A. **76**:572 (Feb. 26) 1921.

[237] Ayer, J. B.: Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Puncture, with Reference to Early Diagnosis of Cord Tumor, Arch. Neurol. & Psychiat. **7**:38 (Jan.) 1922.

(To Be Continued)

American Journal of Diseases of Children

Vol. 27 FEBRUARY, 1924 No. 2

EXTINCTION TESTS IN SCARLET FEVER *

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In 1918, Schultz and Charlton[1] first described the discutient phenomenon, which they obtained after the injection of 1 c.c. of normal or convalescent scarlet fever serum, intradermally, in a scarlet fever patient with a fully developed eruption. According to these writers, a blanching of the skin, together with a complete disappearance of the rash around the injection for an area of from 1 to 2 inches (2.5 to 5 cm.) in diameter occurred within from five to six hours after the injection, and persisted while the scarlatinal rash lasted. In their first series of fifty patients, forty-four gave positive reactions, with five doubtful, and one negative; while patients with other skin rashes when injected with the same serums gave uniformly negative reactions. These authors also pointed out that the injection of serum from patients in the exanthematous stage of scarlet fever did not produce this reaction. This phenomenon was investigated by Hainiss,[2] who in a series of nineteen cases, reports eleven positive and eight negative reactions.

Paschen[3] tested seventy-one cases, sixty-two of which were positive and nine negative, and explains the negative results by saying that the serum was used too late or not injected intracutaneously. He also found that the reaction did not occur with diphtheria antitoxin or with normal horse serum. Tron[4] compared fifty children in different stages of scarlet fever with ninety-nine controls, tested according to the Schultz-Charlton technic, and found an occasionally positive reaction, obtaining only ten definite reactions out of forty-seven frank scarlet fever cases. Steinkopf[5] obtained positive results in 83.7 per cent. of

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* Received for publication, Nov. 26, 1923.

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[1] Schultz-Charlton: Blanching of the Skin by Serum Injection in Scarlet Fever, Ztschr. f. Kinderh. **17**:328, 1918.

[2] Hainiss, E.: Differential Diagnosis in Scarlet Fever, Monatsch. f. Kinderh. **15**:523, 1919.

[3] Paschen, E.: Scarlet Fever Diagnosis, Dermat. Wchnschr. **68**:342, 1919.

[4] Tron, G.: Induced Local Blanching in the Diagnosis of Scarlet Fever, Riforma med. **37**:55 (Jan. 15) 1921; abstr. J. A. M. A. **76**:899 (March 26) 1921.

[5] Steinkopf, C.: Diagnostic Skin Phenomena in Scarlet Fever, Ztschr. f. Kinderh. **31**:132, 1921; abst. J. A. M. A. **78**:156 (Jan. 14) 1922.

forty-nine cases of scarlet fever, and states that the eruption does not merely blanch but that its elements retrogress. Hazelhorst[6] employed the test in fifty undoubted cases of scarlet fever and in thirteen cases of other skin diseases and found that the latter were consistently negative. He also noted that the reaction was negative in as many as 20 per cent. of the cases in which the diagnosis of scarlet fever was certain. He states that the test usually fails to be of any help in the doubtful cases of scarlet fever with slight fever, atypical throats and ill marked or transient rashes.

Mulsow[7] injected thirty patients with convalescent serum obtained from a scarlet fever patient from twenty-one to twenty-eight days after the rash appeared, and found that 53 per cent. gave positive and 10 per cent. questionable reactions. In another series of twenty cases, he injected normal serum and obtained 40 per cent. positive and 15 per cent. questionably positive reactions. He then injected thirty patients with serum taken during the acute stage of scarlet fever and obtained negative results except in one instance, in which the reaction was questionable. He noted the fact that heating the serum had no effect on its reaction. Rojo[8] states that in eighteen of his cases 78 per cent. of the reactions were positive. Schultz[9] reviews this work on the extinction phenomenon. Raymond[10] made 145 injections of normal serum of adults in ninety-seven cases of eruptive fevers and found that 82 per cent. of seventy-two frank scarlet fever cases gave positive reactions. Neuman[11] found that the phenomenon did not occur with foreign serum, distilled water or epinephrin in various high dilutions, and is enthusiastic enough to mention that the diagnostic results border on certainty.

Dorner[12] tested thirty-six cases of scarlet fever in which he got various results, obtaining 85 per cent. positive reactions when the serum was used from patients six weeks after the beginning of the disease. He also calls attention to the fact that when the rash was in decrescendo, results were less marked than when the rash was at its height. He noted that tetanus antitoxin, sheep and rabbit serum did not cause the reaction, and that serum from nurslings unlike any other serum does not blanch. Meyer-Estorf[13] found that the reaction was obtained best when the injection was made on the second day of the rash. Blum[14] injected sixty-four patients with 0.5 c.c. doses and tried to show that the degree of blanching is not dependent on the amount of the injection. He found that hemolysis destroyed the blanching power of the serum. He tested twenty-five cases of definite scarlet fever with varying results and in addition ten cases of surgical scarlet fever, in six of which there was a reaction although all ten were typically positive scarlet fever; in one of the latter, injection of normal serum intradermally gave a negative reaction, i. e., no blanching, while the serum taken during the acute stage from this case when injected into another scarlet fever patient intradermally gave no blanching, i. e., a positive reaction. In another case, the blanching did not come on until forty-eight hours after the injection.

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[6] Hazelhorst, G.: Practical Applicability of Blanching in the Differential Diagnosis of Scarlet Fever, München. med. Wchnschr. **69**:116, 1922.

[7] Mulsow, F. W.: Blanching of the Skin by Serum Injections in Scarlet Fever, J. Infect. Dis. **29**:557 (Nov.) 1921.

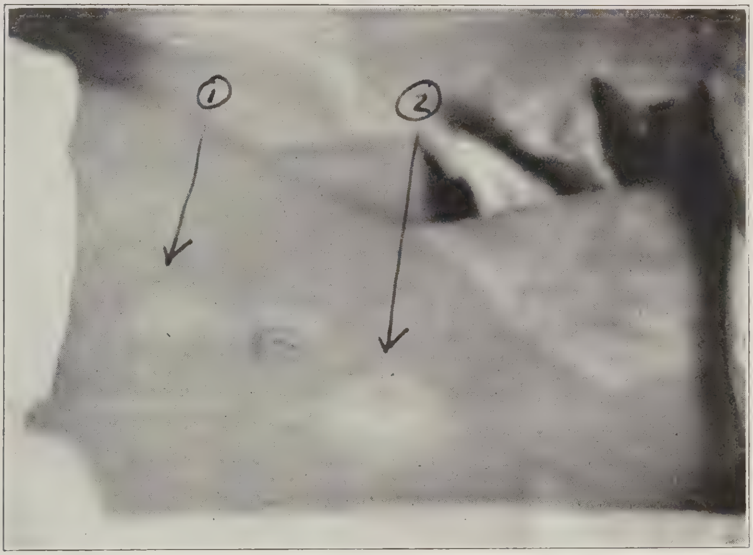
[8] Rojo, D. J.: Extinction Signs in Scarlet Fever, Semana med. **1**:776 (May 11) 1922; abstr. J. A. M. A. **79**:594 (Aug. 12) 1922.

[9] Schultz, W.: Induced Blanching of the Eruption in Scarlet Fever, Acta med. Scandinav. **54**:492 (April 6) 1921; abstr. J. A. M. A. **76**:1544 (May 28) 1921.

[10] Raymond, H.: Differential Diagnosis of Scarlet Fever, Schweiz. med. Wchnschr. **51**:719 (Aug. 4) 1921; abstr. J. A. M. A. **77**:1054 (Sept. 24) 1921.

[11] Neuman, J.: Induced Blanching of the Eruption in Scarlet Fever, Deutsch. med. Wchnschr. **46**:566 (Feb. 12) 1920; abstr. J. A. M. A. **75**:512 (Aug. 14) 1920.

[12] Dorner, G.: Extinction Tests in Scarlet Fever, Med Klin. **17**:1543, 1921.



There were two definite responses in this patient to normal serum from different individuals and, in this instance, from different type groupings.

Marie[15] calls attention to the fact that injections of epinephrin in solution of 1 : 12,000,000 do not cause the discutient phenomenon.

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[13] Meyer-Estorf: Further Remarks Regarding Scarlet Fever Extinction, Med. Klin. **17**:526 (May 1) 1921.

[14] Blum, J.: Extinction Phenomena in Scarlet Fever Diagnosis, München. Med. Wchnschr. **69**:466 (March 31) 1922.

[15] Marie, P. L.: The Schultz-Charlton Phenomenon of Extinction and the Diagnosis of Scarlet Fever, Presse méd. **29**:1001, 1921.

Wöhlisch and von Mikulicz,[16] Salevsky[17] and Mouriquand[18] agree with the general findings of other authors.

As can be seen, there is great difference of opinion as regards the efficacy of the test, some authors claiming that it is specific, others that it is worthless. It occurred to us that further work should be done in order to evaluate this sign, as any procedure which would lead to a diagnosis in the borderline case of scarlet fever would be of distinct value.

We tested fourteen cases of definite scarlet fever at the height of the rash, using the following solutions: epinephrin 1:1,000; stock typhoid, triple vaccine; physiologic sodium chlorid solution; horse serum and serum from a convalescent case of about three weeks' duration. One-half cubic centimeter doses were used. Table 1 gives the results, positive indicating blanching; negative, no blanching.

TABLE 1.—*Results of Tests in Fourteen Cases*

	Epinephrin 1:1000	Typhoid Vaccine	Normal Serum	Horse Serum	Convalescent Scarlet Fever Serum
Positive...........	14	0	0	3*	3
Negative..........	0	14	14	11	11

* Questionable, but included in positive results.

TABLE 2.—*Results of Eight Tests*

	Positive	Negative
Normal human serum, 1 c.c.	7	1
Horse serum, 1 c.c.	0	8

Epinephrin produced blanching in all cases. The reaction, however, differs from that produced with human serum in that it begins in a few minutes and disappears in from five to six hours; the blanched area is much paler than normal skin, and is surrounded by a definite red margin from 3 to 5 cm. wide. Epinephrin was then injected in several diphtheria patients and the same result was obtained, lacking the contrast of the surrounding scarlet skin. The blanching obtained with human serum appears in from six to eight hours and persists until the rash fades. The area varies in size from 2 to 10 cm. in diameter, is round or oval, and may be definitely delimited from the surrounding erythematous skin, or may show an irregular indefinite margin. In some of the reactions, slender fingers of blanched skin extend into the rash even as far as from 8 to 10 cm.

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[16] Wöhlisch, E., and von Mikulicz Radecki: Skin Blanching Tests, Berl. klin. Wchnschr. **58**:389, 1921.

[17] Salevsky: Discutient Phenomenon, M. J. No. 1, quoted in Zentralbl. f. d. Ges. Kinderh. **15**:33 (July 10) 1923.

[18] Mouriquand: Scarlet Fever Signs, J. de méd. de Lyon **3**:66, 587, 1922.

Foreign protein in the form of stock typhoid vaccine and horse serum produced no typical blanching; although there were three instances of horse serum injection in which a rather indefinite disappearance of the rash occurred about 2 to 3 cm. in diameter. If these reactions were typical, a test which showed only three positive reactions out of fourteen experiments would be of little value. When we tested an additional eight cases of scarlet fever with horse serum and with convalescent scarlet fever serum, using a different serum than that used in the first experiment, we were surprised to find seven positive reactions out of eight as tabulated in Table 2, indicating that not all normal serums have the same power of blanching, a fact more evident from later experiments.

Normal serum was then compared with serum from a convalescing scarlet fever patient in the fourth week of the disease, and gave a higher percentage of positive reactions, as can be seen from Table 3.

Table 3.—*Results of Fourteen Tests*

	Positive	Negative
Normal human serum, 0.5 c.c.	9	5
Convalescent scarlet fever serum, 0.5 c.c.	3	11

Table 4.—*Results of Twenty-Seven Tests*

	Positive	Negative
Normal human serum, 1 c.c.	22	5
Convalescent scarlet fever serum, 1 c.c.	17	10

Most observers state that like reactions are obtained with serums in 0.5 c.c. and 1 c.c. amounts. To determine whether the amounts of serum influenced the results, twenty-seven cases of scarlet fever were tested, 1 c.c. each of normal and convalescent fever serum being employed. That a higher percentage of positive results can be obtained with the larger amount is shown in Table 4 as compared with the preceding table, consequently this amount was used in all subsequent experiments. Some observers have noted trauma when amounts larger than 0.5 c.c. are used, but we did not see in any case that the reaction was adversely influenced by injection of the larger amount.

An additional series of eight cases were then tested, normal and convalescent serum in 0.5 and 1 c.c. amounts being employed, with the following results:

Table 5.—*Results in Additional Series of Eight Cases*

	Positive	Negative
Normal human serum, 0.5 c.c.	4	4
Convalescent scarlet fever serum, 0.5 c.c.	0	8
Normal human serum, 1 c.c.	5	3
Convalescent scarlet fever serum, 1 c.c.	4	4

While few cases were tested in this manner, the results favored the larger amount for the test.

The following cases were tested by the intradermal injection of 1 c.c. of normal human serum: measles, six; diphtheria bacillus carriers with erythematous rashes, one; influenza with erythematous rash, two; urticaria, one; drug rash, one; serum rash, one; erythematous rash following administration of arsphenamin, one. There was no area of blanching in any instance. Two patients who had measles were injected with adrenalin, and blanching occurred in one.

Serum from definite scarlet fever cases during the first week of the disease was injected in eighteen cases, normal human serum being employed for control, with the following results:

Table 6.—*Results of Eighteen Tests*

	Positive	Negative
Normal human serum, 1 c.c.	18	0
Acute scarlet fever serum, 1 c.c.	0	18

Owing to the persistent negative results obtained when serum from a scarlet fever patient during the first eight to fourteen days of the disease is used, this test is of considerable value in establishing a diagnosis in doubtful cases. Serum from two patients, hospital orderlies who had been exposed to scarlet fever and who developed sore throats and were isolated as possible scarlet fever cases, was injected intradermally in a known case at the height of the rash. In both instances, blanching occurred, and the subsequent course confirmed the opinion that they were not developing scarlet fever. In another case, the serum of a nurse who was exposed in one of the scarlet fever wards and who developed a sore throat, nausea and vomiting associated with a slight erythema, was injected into a scarlet fever patient with a fully developed rash, and blanching was produced. The final diagnosis after twenty days' observation was acute streptococcic sore throat.

Serum from five cases of suspicious but not well defined scarlet fever was injected into the same number of cases of acute scarlet fever at the height of the rash, the reactions being negative in each case. Later, the diagnosis of scarlet fever was verified in these cases by the subsequent findings, extensive peeling, etc. The serum of two control cases of streptococcus sore throat was injected intradermally into two scarlet fever patients at the height of the rash, with negative results, i. e., with blanching. In one instance, the patient, a physician on service at the hospital, developed symptoms of a mild scarlet fever. We had on hand some of his blood serum which we had used in some other work, serum which had been withdrawn about four weeks prior to his illness. This was used as a control in testing out the blanching power of serum withdrawn from him on the second day of his illness. The latter gave no reaction while the old serum caused definite blanching.

The observation has been made by others, and we have found it true in our cases, that serum from different healthy individuals produced different degrees of blanching. However, no explanation has been brought forth. To determine whether the iso-agglutinins and the hemolysins contained in the serum used and the blood of the patient had any influence on the degree of blanching, we obtained two sets of serums of the four types and tested fifteen patients with the first set and ten with the second. Jansky's classification is used in designating the different blood groups. The symbols (—) and (+) are used to express the degree of blanching.

Table 7.—*Results of Employment of Various Types of Serum on Different Types of Patients*

	Type of Serum Used for the Test			
Type of Patient	1	2	3	4
1	±	++	++++	+++
1	—	—	++++	+++
1	—	++	++++	+++
1	+	—	++++	—
2	—	++	+++	—
2	—	++	++++	++
2	—	++	++++	+++
2	+	++	++++	+++
2	±	±	+++	± (?)
2	++++	++	+++	+++
2	++	—	+++	—
3	+	±	+++	+++
3	++	+++	++++	++++
3	—	++	+++	++++
4	—	—	+	++

Table 8.—*Results of Employment of Various Types of Serums on Different Types of Patients*

	Type of Serum Used			
Type of Patient	1	2	3	4
1	—	+++	—	++
1	—	++	±	+
3	—	+++	±	++
3	+	+++	±	++
1	—	+	—	+
2	—	+++	—	++
1	—	++++	—	++
1	±	++	±	+
2	—	+++	—	++
1	+	++++	—	+

From results obtained, as shown in Table 7, it was seen that there were 100 per cent. positives in this series when the four types of serum were used. We also saw that Type 3 of this series caused the greater number of positive reactions in the greater degree; we also noted that if normal Type 1 serum of this experiment had been used alone there would have been only six definite reactions out of fifteen;

therefore, not all normal serums have the same blanching effect. We were interested to find out whether the second series of cases with various type serums would give the same number of positive reactions, especially with a new Type 3.

In the group findings presented in Table 8, Type 2 caused the greatest number of reactions.

A study of the foregoing tables discloses no relation between the degrees of blanching obtained and the blood groups of the patient and donor. It does, however, show that the serums from certain individuals persistently cause definite and marked blanching when injected intradermally in scarlet fever cases at the height of the rash, while those from other individuals produce blanching to a less degree or in some cases not at all.

A study of Tables 7 and 8 shows that the Types 2 and 3 used, caused the greatest number of reactions, Type 2 of Table 8 and Type 3 of Table 7. To see whether Type 2 of Table 8 and Type 3 of Table 7 would be positive, or produce blanching in the same individual, ten patients in the acute stage of scarlet fever were injected with Types 2 and 3 of Tables 7 and 8, with the following results:

TABLE 9.—*Results Obtained with Various Types of Serums*

Type of Serum Used for the Test			
Type 2 of Table 8	Type 2 of Table 7	Type 3 of Table 8	Type 3 of Table 7
±	+	+++	++
+	—	—	—
+	+	—	—
+	+	—	±
—	++	+++	—
±	+	++	—
—	±	+++	±
±	+++	+	—
—	++	++	±
±	+++	++	+

From the findings presented in Table 9, it can be seen that when a type serum is definitely positive, it is consistently positive, irrespective of the blood grouping of the patient or donor.

There have been as many theories as to the cause of this reaction as there have been men working on the problem. Meyer-Estorf [13] injected albumin serum and globulin serum intradermally and noticed no difference in the reaction; both caused blanching, but the number of cases studied was not impressive. He states that the exanthem is due to a hyperemia and that the extinction is due to a vascular constriction which Buschmann claimed that he had observed under the microscope. He assumes the presence of an antibody in the extinction serum, and points out the fact that animals which are immune to scarlet fever have no antibodies for scarlet fever, and when their serum is used for the test there is for that reason no blanching of the skin. Raymond, quoted by Dorner,[12] thought that the vasoconstrictor action was due to epinephrin, but Dorner remarks that this could not be true since the points of blanching are not paler than normal skin, whereas epinephrin causes an extreme pallor. He, as well as Paschen,[3] believes that the scarlet fever serum has a vasodilatory action and that normal serum destroys this property. Dorner also calls attention to the significant fact that infant's serum does not cause any blanching. Hainiss, quoted by Blum,[14] stated that the normal serum lost its blanching power when rendered inactive. However, our experience, as well as that of others, would seem to indicate that the thermolabile factor had nothing to do with the reaction. Hemolysis destroys the blanching effect (Blum [14]). Marie states that the reaction is due to the albumins in the serum, the globulo-albumin and the seralbumin.

It has been considered by some that the blanching is due to a local immunity connected with the presence of antibodies in the normal serum. Schultz-Charlton states that the effect was not obtained from normal serum from which the proteins had been precipitated out by ferric-chlorid, and propounded the theory that the human serum contains inhibitory substances which act either on the vasodilatory principle of the scarlatinal virus or on the blood vessels directly. Wolf-Eisner, quoted by Meyer-Estorf,[13] seeks to explain the extinction phenomena along the lines of biologic immunity. He proceeds from Pirquet's theory of the cause of scarlet fever, which attributes the cutaneous manifestations of the disease to a meeting of antibodies in the skin, and relates the phenomenon to other immunity reactions as that of the tuberculins. No theory brought forth as yet definitely explains the phenomenon in question. What this substance is is not known, but its importance warrants further study.

SUMMARY

One hundred and thirty-three scarlet fever cases were studied and compared with twenty-two control cases in an attempt to evaluate the extinction phenomenon of Schultz-Charlton. We were able

1. To confirm the fact that injections of serum from acute cases of scarlet fever, injected intradermally in another case of acute scarlet fever in the exanthematous stage will not cause blanching.

2. To show that not all serums are similarly potent in producing blanching, few normal serums producing no blanching at all, a fact which limits the application of this test in its negative phase.

3. To show that the injection of normal serum in cases with rashes other than the scarlet fever rash does not cause the reaction.

4. To show that normal serums give a greater number of reactions than convalescent scarlet fever serum.

5. To show that normal serums in 1 c.c. amounts give a greater number of positive reactions than normal serums in 0.5 c.c. doses.

6. To point out that if the serum is used and produces a definite reaction in one case, it will produce the same reaction in nearly 70 per cent. of other cases tried.

7. To point out that if two serums are used which produce definite blanching in a given case, they will complement each other and will give 100 per cent. reactions in other cases tried.

CONCLUSIONS

1. There is present in the blood of some normal and some convalescent scarlet fever serums a substance which, when injected intradermally, will cause the rash of scarlet fever to disappear at the seat of the injection, as first pointed out by Schultz-Charlton.

2. The serum from an acutely ill scarlet fever patient in the erythematous stage will in the great majority of cases not cause a disappearance of the rash when injected intradermally into another acutely ill scarlet fever patient in the erythematous stage.

3. The cause of this reaction is not known.

ENTEROLITH AS CAUSE OF CHRONIC OBSTIPATION IN A BREAST-FED INFANT *

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AND

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True intestinal stone in early life is rare. We were unable to find any reported in a child under 6 years of age. The case to be described occurred in an infant exclusively breast-fed, who suffered complete obstruction, and was operated on, at the age of 8 months.

REPORT OF CASE

History.—W. J., a boy, aged 8 months, had been fairly well nourished on the breast, with a monthly gain of 1 pound (453.6 gm.). He had never had an unassisted bowel movement. Meconium was evacuated for first two weeks by rectal irrigation, and fecal matter was not seen in the stool until after the infant was 2 weeks old, when hard fecal masses began to be obtained by irrigation. When castor oil was given, the stools would be liquid, and on one occasion blood was present in stool. During the eight months of the obstinate constipation, numerous laxatives, including croton oil, were tried by the attendant, often unsuccessfully for several days at a time. At no time was magnesia given. Diarrhea resulted on two occasions, between the ages of 6 and 7 months. The only other complications were eczema for a few weeks in the early months, and abdominal distension most of the time.

At 8 months of age, the infant developed fever (2 degrees) and the appetite failed, but he took water eagerly. Vomiting occurred twice daily. On the third day of illness, May 31, 1923, the patient came under our observation at St. Luke's Hospital.

Examination.—At this time, the weight was 17 pounds (7.7 kg.). The infant had an anxious expression, and the eyes were somewhat sunken. The temperature 102. The abdomen was markedly distended, so that palpation was difficult. No roentgenogram was taken before barium sulphate was administered. This was unfortunate, as it would have been of value to learn whether a shadow was cast by the intestinal mass independently of the barium sulphate. However, a barium sulphate enema did not pass the sigmoid flexure; a barium sulphate meal required forty-eight hours to traverse the intestinal tract, and there was barium sulphate still present in the colon and sigmoid at the end of 120 hours. In the middle portion of the sigmoid, an area of 1½ inches was less opaque than the surrounding structures. Under anesthesia, a hard globular mobile mass was easily felt in the region of the umbilicus and diagnosed as an enterolith.

Preoperative Laboratory Findings.—Examination of the blood revealed: leukocytes, 23,200; polymorphonuclears, 47; large lymphocytes, 5; small lymphocytes, 47; transitionals, 1.

In the urine, there was a trace of bile and an occasional pus cell, but no blood. A few granular casts and cylindroids, and a number of uric acid crystals were noted, but no indol was present.

Operation (E. L. M.).—A right rectus incision, 1½ inches above and 2½ inches below the umbilicus was made, with delivery of a redundant loop of sigmoid much enlarged in length and in caliber. The mass could be moved

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* Received for publication, Oct. 31, 1923.

slightly in both directions within the bowel. A longitudinal incision was made at the lower end of the bowel and a stony mass was expressed. The intestinal wall was thickened. Closure of the sigmoid and abdominal opening was without incident.

Course.—The infant had a normal convalescence, with the exception of the need for assistance in bowel evacuation, for which suppositories were used.

Five days after operation, the blood showed a relative and actual increase in the neutrophiles: white cells, 18,200; polymorphonuclears, 79 per cent.; large lymphocytes, 2 per cent.; small lymphocytes, 19 per cent.

The wound healed normally, and no elevation of temperature was present after this time. The infant was taken from the hospital one week after the operation.

Specimen.—The stone was oval, 3½ by 5 cm.; weighed 40 gm., and was dark gray and smooth. When cut through, the outer portion was laminated, stony, unyielding, the center was less dense, smooth and gray, and contained no nucleus of any different composition. When kept in specimen jar solution for several months, the exterior of the stone eventually softened and crumbled into the solution, forming a dirty grayish opaque mixture. Analysis [1] of the stone showed that the ash consisted principally of calcium (50.51 per cent.), magnesia (3.19 per cent.), and phosphorus (18.44 per cent).

Outcome.—Two months after the removal of the stone, the infant had gained 2½ pounds (1,134 gm.). The bowels had not moved voluntarily, and a mild laxative or an occasional suppository was required. The child was still on the breast, and weaning was advised, so as to provide food with more residue.

OCCURRENCE

Inspissated and impacted meconium as a cause for fetal or newborn obstruction has been reported by Bullowa and Brennan.[2] Their case, in an infant 2 days old, came to necropsy, and the obstructive mass was found to consist of white, inspissated, impacted and stratified meconium, evidently of intrauterine origin.

Fecal impaction is of more common occurrence. It is probable that, in most cases, the mass remains a fecalith, or that a nucleus of a foreign body gains accretions from the feces or from the mineral excretions of the intestinal mucosa. Dorning reported a fecal impaction in a 2-year-old child due to the swallowing of particles of cloth, and he believes that insoluble mineral substances, such as magnesia or bismuth, when taken over a long period may accumulate and form an obstruction.[3]

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[1] Analysis was made by Drs. Walter M. and Roy Cross. The hypothetical combination of the ash was as follows: Calcium phosphate $(Ca_3\,PO_4)_2$, 40.35 per cent.; calcium carbonate $(Ca\,Co_3)$, 51.33 per cent.; magnesium carbonate $(Mg\,CO_3)$, 6.83 per cent. The organic matter other than fat and cholesterol most probably existed as fatty acids combined with the lime and magnesia of the ash as lime and magnesium soaps.

[2] Bullowa, J. G. M., and Brennan, R. E.: Intra-Uterine Intestinal Obstruction from Inspissated and Impacted Meconium, J. A. M. A. **73:** 1882 (Dec. 20) 1919.

[3] Dorning, John: Intestinal Obstruction in Early Life, Med. Rec. **45:** 556, 1894.

Shattock states that there are only three specimens of intestinal calculus in the human collection at the Royal College, London. A few instances are recorded in which the obstinate constipation of adults, which had existed since childhood, was due to an enterolith. Simpson [4] reported an enterolith in a 16-year-old girl in Scotland, who, as a child, had been in the habit of chewing heather while herding cattle. The enterolith was 4½ by 2¾ inches (11.3 by 6.9 cm.), and was composed of heather roots and twigs compressed and surrounded by mineral accretions of stony hardness. The mass was in the ileum, 16 inches

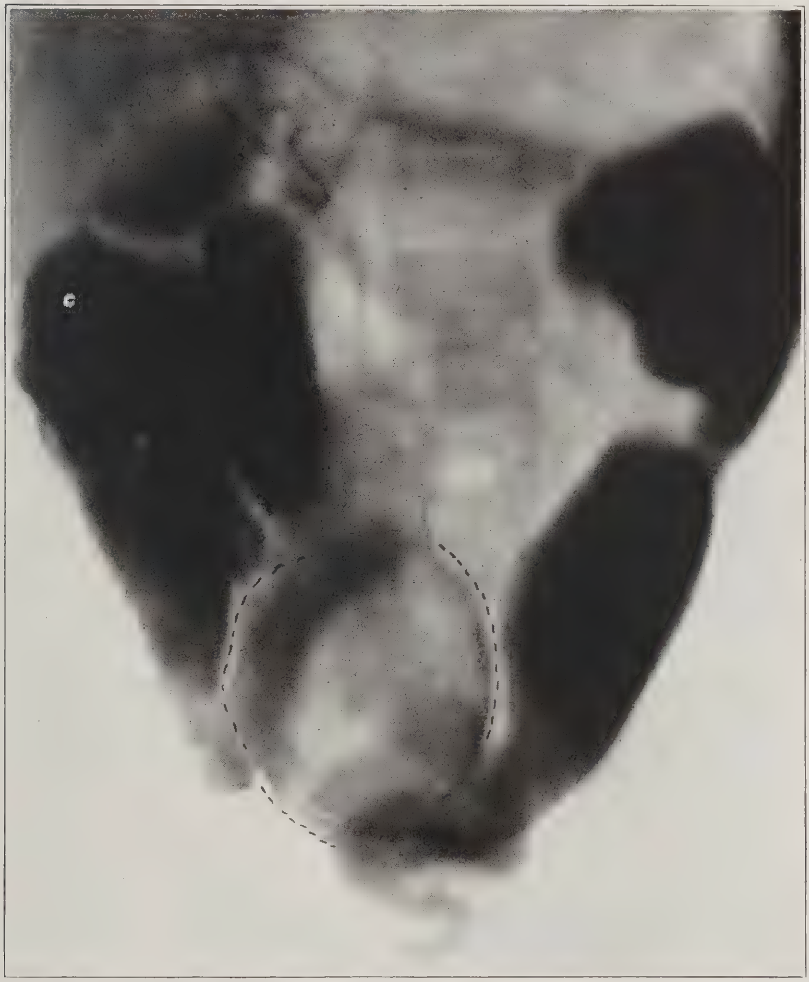

Fig. 1.—Enterolith in sigmoid flexure. The oval mass is within the dotted line.

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[4] Simpson, B. S.: Edinburgh M. J. **30:** 176 (April) 1923.

above the ileocecal valve. It is interesting that stones, avenoliths, formed from ingested oatmeal, were noted in Scotland.[5]

Boardman[6] described his case, in an adult, as beginning in infancy while the child was being fed on the breast.

Enteroliths are not mentioned in acute intestinal obstruction in young children. Peterson[7] had fifty-five such cases, mostly in infants, one of which was due to a foreign body, not an enterolith. Gant[8] has collected fifty-four cases, the three youngest patients being between 6 and 8 years.

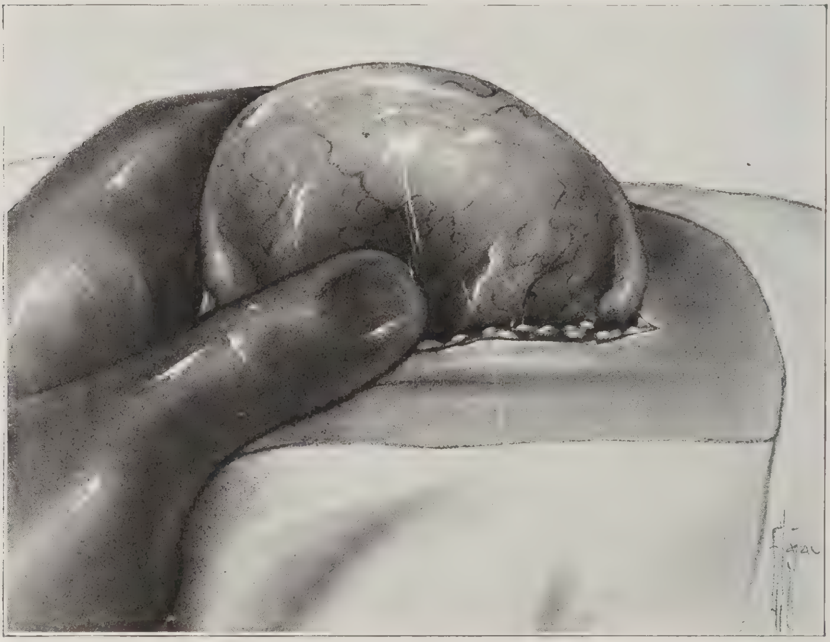

Fig. 2.—Sigmoid, showing distension by stone, at time of operation.

Treves ("Intestinal Obstruction") divides enteroliths as to composition into (1) concretions formed of phosphate of lime or magnesia, or of triple phosphates or of mixtures of these salts; (2) "oat-stones" of low specific gravity composed mostly of vegetable matter, fecal matter and calcareous material, and (3) concretions formed of insoluble mineral matter which has been swallowed as medicine, mostly magnesia.

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[5] In a personal communication, Leonard Findlay, Glasgow, said that he has not known of an enterolith in children in Scotland.

[6] Boardman, W. W.: Am. J. Roentgenol. **10**:369 (May) 1923.

[7] Peterson, E. W.: Surg., Gynec. & Obst. **35**:436 (Oct. 22) 1923.

[8] Gant, S. G.: Diseases of Rectum, Anus and Colon, Philadelphia, W. B. Saunders Company **2**: 494, 1923.

COMMENT

Formation.—While stones may develop in early life, there is a history of long-standing constipation and many years elapse [9] before the stone reaches the complete obstructive size or situation, in practically all cases in adult life. In the case here reported, no magnesia, no bismuth and, until the time of operation, no barium had ever been administered. There was a history of difficult evacuation of the bowel since birth, and a prolonged period of meconium stools, with no fecal matter appearing for two weeks. There had been no jaundice at any time. The nucleus had evidently been formed during intrauterine life or shortly afterward, and contained no foreign body. Inspissated meconium, dehydrated feces and accretions from the secretions of the intestinal mucosa offer, it seems to us, the only explanation of intestinal calculus in our case. The possibility of the origin in a diverticulum is of theoretical interest.

Mechanism.—The mechanism of stone formation and retention is interesting, and is not entirely understood. Young children swallow many indigestible bodies of various sizes, sometimes exceeding the usual circumference of the intestine. Such foreign bodies are usually passed finally, or may remain for some time in the bowel, usually the rectum, without mineral accretions. It is difficult to understand why peristalsis, which may even become increased by the presence of the stone, does not pass the mass while it is yet small.[10] Fecal matter will be pushed past the stone without dislodging or evacuating it. In the reported cases, most stones are found in the rectum. In our case, the stone was found in a favorable location—a flexure, where, by its ball-valve action, liquid feces were at times permitted to pass.

Diagnosis.—Obstinate constipation is of first importance and is the cause for seeking medical advice. The general symptoms are likely at times to be stormy, and are sufficient to suggest an acute obstruction: vomiting, periods of distress and anxiety, tenderness, colic, distension and flatulence, peristaltic wave and diarrhea with mucus, blood or pus. So rare is the intestinal stone and so difficult is palpation of the mass that stone is not considered until the individual comes to operation, or a roentgenographic examination is made. Under anesthesia, it was possible in our case to feel the tumor through a relaxed abdominal wall, but the roentgenogram is essential for differentiation. As has been suggested by Pfahler,[11] the stone, if of sufficient density, should first be sought by a roentgenogram without a barium sulphate coating, and, if this procedure is inconclusive, the opaque meal will outline the mass, which of itself may be of insufficient density to cast a shadow.

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9. Cowan, J. F.: Enteroliths, S. Clinics of N. Amer. **2**:401 (April) 1922.
10. Boardman, W. W.: Am. J. Roentgenol. **10**:369 (May) 1923.
11. Pfahler, G. E.: Diagnosis of Enteroliths, Surg. Gynec. & Obst. **21**:14. 1915.

REPORT OF A CASE OF HEALED MILIARY TUBERCULOSIS *

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FREDERICK, MD.

The pathologic examination in a case of generalized miliary tuberculosis in childhood shows why this disease is nearly always fatal. There is a softened focus of tuberculosis, usually in a lymph node, which has discharged into a blood vessel, not once, but several times, the cavity having undoubtedly filled. Evidence of repeated infection is found in the size of the resultant tubercles. There are crops of different sizes, but the tubercles that belong to one crop are of approximately the same size. This indicates an eruption of tubercle bacilli into the blood stream at different intervals. The discharge of tubercle bacilli may be so overwhelming and produce so extensive and generalized an infection as to prove fatal in a short time. But if it does not, successive discharges of tubercle bacilli can hardly be borne; and, from the nature of the lesion in the tuberculosis focus, successive discharges are the nearly invariable rule.

It is conceivable that the focus of dissemination may be so small that the number of tubercle bacilli discharged may not produce a severe infection, and healing of the focus, after it has been evacuated, may rapidly take place. Under such conditions, the infection, while generalized, may not be sufficient to overwhelm the organism, and recovery may occur. I wish to report what appears to be an example of healed miliary tuberculosis.

REPORT OF CASE

History.—N. D., a white boy, aged 11 years, admitted to the Harriet Lane Home, Oct. 21, 1919, the youngest of four children, all the others being well, and whose father had had asthma for many years, was breast fed for a year and developed normally. At 1 year of age, he had measles followed by "catarrhal croup," during which he had difficulty in getting his breath. Following this, he had attacks of shortness of breath, at first every month or two, and continuing up to the present time, though at rather longer intervals. These attacks were brought on by cold, excitement or violent exertion, or when the patient was in a room where there was much tobacco smoke. The adenoids and tonsils were removed at the age of 5. At 8 years of age, the boy had pertussis; at the age of 10, influenza followed by pneumonia. He was brought to the hospital because of the asthmatic attacks, and remained for five days. The temperature during this time was normal.

Physical Examination.—The boy was moderately well developed, somewhat underweight, weighing 59 pounds (26.8 kg.). The lungs on percussion were normal. On auscultation, a few scattered moist râles were heard. The heart

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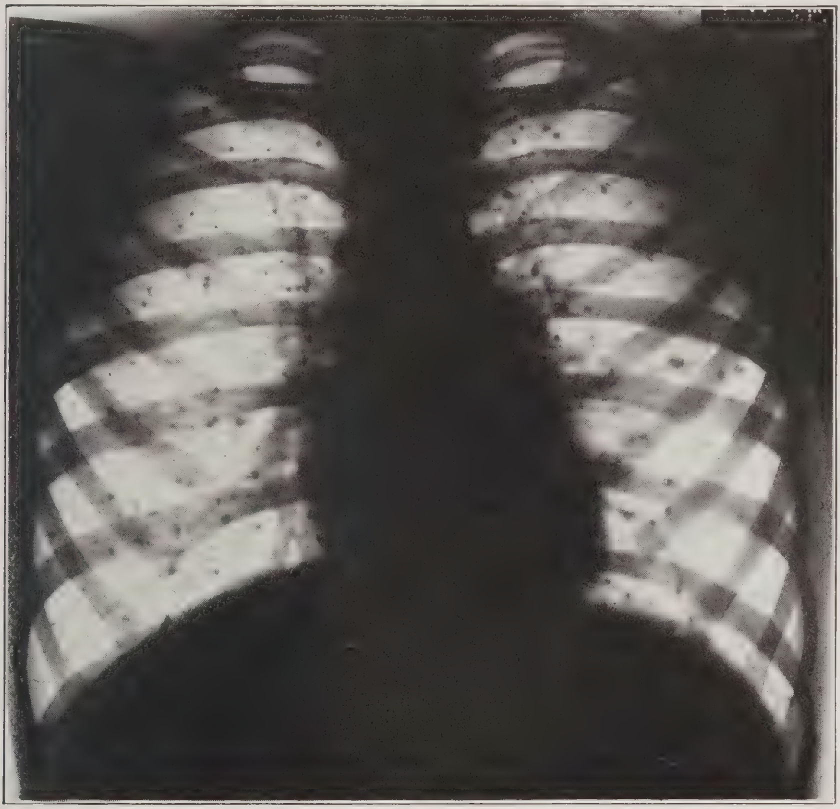
* Received for publication, Sept. 26, 1923.

* From the Department of Pediatrics, Johns Hopkins University.

was normal. An intracutaneous injection of tuberculin, 0.1 mg., produced no reaction. A roentgenogram of the chest revealed small opaque areas scattered throughout both lungs even to the margins. There was no evidence of an accumulation of these in the vicinity of the roots of the lungs. Stereoscopic plates showed that the nodules were situated in the lung substance. The nodules were, roughly, uniform in size and appeared to be small areas of calcification. Roentgenograms of other portions of the body showed nothing similar.

Course.—The boy has been under observation for nearly four years. His health has remained good. His asthmatic attacks are infrequent. Several recent roentgenograms show exactly the same picture as did the first. Subsequent tuberculin tests were made. There was a definite reaction on injection of 5 mg. of tuberculin intracutaneously.



Appearance of chest, showing calcified nodules scattered through both lungs.

The wide and even distribution of the nodules point to a dissemination by the blood stream rather than by the bronchi or lymphatics. The possibility of metastases of some primary undiscovered tumor has been eliminated by the length of time that has elapsed. It seems that the presence of several nodules, presumably calcified, can be accounted for most satisfactorily by assuming that the boy at some time, following measles or pneumonia, had an eruption of tubercle bacilli into his blood that caused a number of isolated lesions; but the infection was overcome, as there was no recurrence. Subsequently, calcification of the lesions took place. Miliary tuberculosis in adults, running a chronic course or unsuspected until detected by roentgenograms, has been reported recently by Bierman [1] and by Stivelman and Hennell.[2] I have seen an example of the form described by the latter authors. Unsuspected and healed miliary tuberculosis in a boy of 14 years, with death occurring from quite a different cause, has been reported by Opie and Andersen.[3] The roentgenograms taken postmortem of the lungs of this child are strikingly similar to those of my patient. This fact, taken in connection with the positive tuberculin reaction, renders the diagnosis reasonably certain.

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1. Bierman, M. I.: Minnesota Med. **5**:661-665 (Nov.) 1922.
2. Stivelman, B. P., and Hennell, Herman: J. A. M. A. **80**:536 (Feb. 24) 1923.
3. Opie, E. L., and Andersen, H.: Am. Rev. Tuberc. **4**:629 (Nov.) 1920.

TUBERCULOSIS OF THE TONSILS AND ADENOIDS

A CLINICAL AND ROENTGEN-RAY STUDY OF FIFTY CASES OBSERVED FOR FIVE YEARS AFTER OPERATION *

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Since 1912, every tonsil and adenoid removed at operation in the Johns Hopkins Hospital has been studied histologically. While no attempt is made to examine the entire tonsil or adenoid by serial sections, the blocks selected for microscopic section and the number of slides obtained for study are uniform throughout the whole series of 3,260 cases. This paper deals entirely with those cases in which a tuberculous lesion was discovered in the tonsil or adenoid; other pathologic conditions of a nontuberculous nature that were noted in this study will be presented in a subsequent publication.

Virchow,[1] in 1864, made the statement that tuberculosis of the tonsil is a rare occurrence, and that this tissue is extraordinarily immune to tuberculous infection. For a period of fifteen years following Virchow's publication, no experimental or pathologic observations were made on tuberculosis of the lymphoid tissue in the pharynx, with the exception of an occasional note on the ulcerative lesions in this region that occur in the late stages of pulmonary tuberculosis. During the course of some experimental observations on the effect of feeding tuberculous meat, Orth,[2] in 1879, observed ulcerated tuberculous lesions in the tonsils. Baumgärten[3] repeated the feeding experiments of Orth five years later, and noted, in addition to the lesions in the tonsils, a tuberculous cervical adenitis. He commented on the resemblance of the condition in these glands to scrofula, but was confused because a tuber-

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* Received for publication, Nov. 6, 1923.

* From the Department of Surgery of the Johns Hopkins University and Hospital.

* Many of these references were made possible through the aid of the Surgeon-General's Library.

[1] Virchow, R.: Die krankhaften Geschwülste **2:**674, 1864.

[2] Orth, J.: Experim. Untersuchungen über Fütterungstuberculose, Virchows. Arch. f. path. Anat. **76:**217, 1879.

[3] Baumgärten: Ueber die Uebertragbarkeit der Tuberkulose durch die Nährung und über Abschwächung der pathogenen Wirkung der Tuberkelbacillen durch Faülnis, Centralbl. f. d. med. Wissensch. **22:**347, 1884.

culous cervical adenitis in man is found so rarely in association with an advanced pulmonary lesion.

Lermoyez,[4] Cornil[5] and Abraham[6] were among the first to present clinical cases of tuberculous tonsils and adenoids removed at operation. Lermoyez, in 1894, removed the adenoids in a child, aged 6 years, who

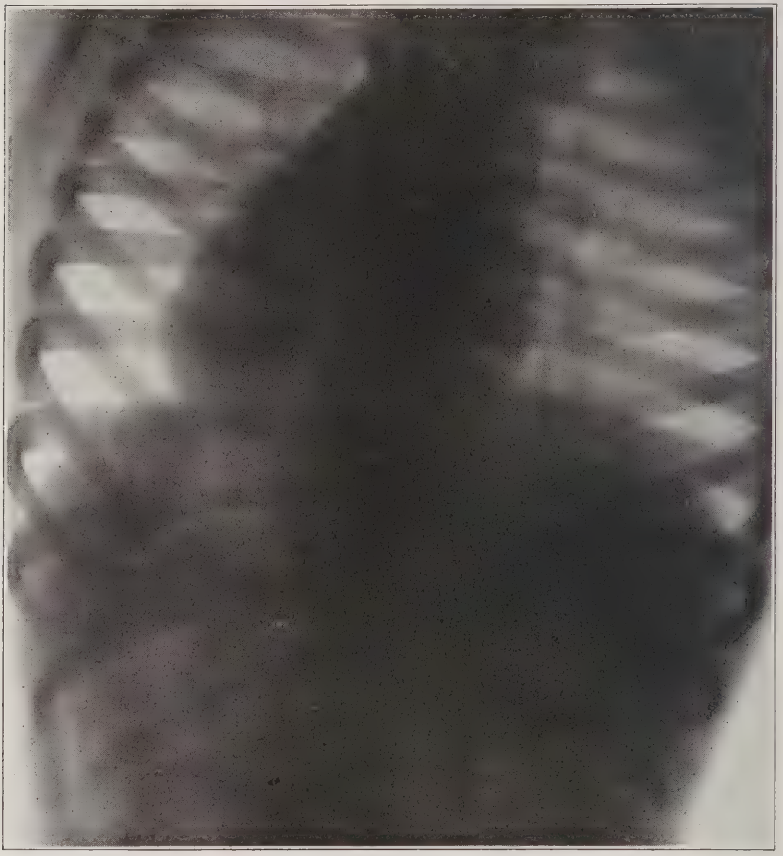

Fig. 1.—J. H., colored boy, aged 4, two and a half years after operation. The lungs were clear. The mediastinal glands were enlarged, the condition suggesting mediastinal tuberculosis. At the time the roentgenogram was taken the child was admitted to the hospital for acute nephritis. Aside from edema, the physical examination was negative. Both tonsils and adenoids and the cervical glands on the left side were found to be tuberculous two and one half years ago.

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[4] Lermoyez, Marcel: Des végétations adénoides tuberculeuses du pharynx nasal, Bull. et mém. Soc. méd. d. hôp. de Paris **11**:559, 1894.

[5] Cornil, V.: Sur l'angine tuberculeuse, J. d. conn. méd. prat. **42**:193, 1875.

[6] Abraham, P. S. Tubercle of the Tonsils, J. Acad. Med. Ireland **3**:358, 1885.

had no clinical evidence of tuberculosis in the lungs or elsewhere in the body. He found tubercles in the adenoids and was able to demonstrate tubercle bacilli in the lesion.

During the period from 1885 to 1900, Orth,[7] Krückmann,[8] Schlänker,[9] Ruge[10] and Friedmann[11] reported postmortem examina-

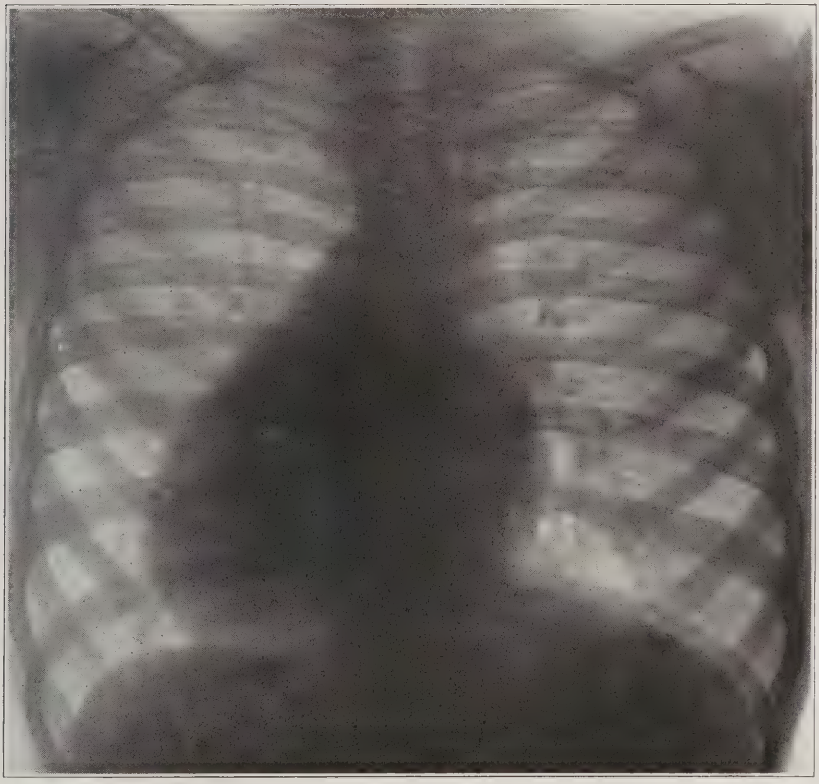

Fig. 2 (J. H.).—Appearance of chest of patient two years later. The lungs were still clear. There was a decided reduction in size of the mediastinum. The physical examination was negative. The cervical adenitis cleared up within a year after the operation. The child received tuberculin treatment for one year after operation.

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[7] Orth, J.: Lehrbuch der spec. patholog. Anat., Berl., 1889, Ib, 663.

[8] Krückmann, E.: Ueber die Beziehungen der Tuberkulose der Halslymphdrüsen zu der Tonsillen, Virch. Arch. f. path. Anat. **134**:534, 1893.

[9] Schlänker, E.: Untersuchungen über die Entstehung der Tuberkulose der Halsdrüsen, besonders über ihre Beziehungen zur Tuberkulose der Tonsillen, Virchows. Arch. f. path. Anat. **134**:161, 1893.

[10] Ruge, H.: Die Tuberkulose der Tonsillen vom klin. Standpunkte, Virchows Arch. f. path. Anat. **144**:431, 1896.

[11] Friedmann, F.: Ueber die Bedeutung der Gaumentonsillen von jungen Kindern als Eingangspforte für die tuberkulöse Infection, Beitr. z. path. Anat. u. z. allg. Path. **28**:66, 1900.

tions in which tuberculous lesions were found in the tonsils. In Friedmann's cases, no tuberculosis was found elsewhere in the body; in the others, the cervical glands were involved, but the microscopic appearance indicated that the tonsillar lesion was the most advanced and apparently the primary portal of entry. Dmockowski,[12] in 1891, experimentally infected the tonsils and cervical glands, and demonstrated, in microscopical sections, the tubercle bacillus in the tonsils, the cervical glands and the intervening lymph channels. Dieulafoy,[13] in 1895,

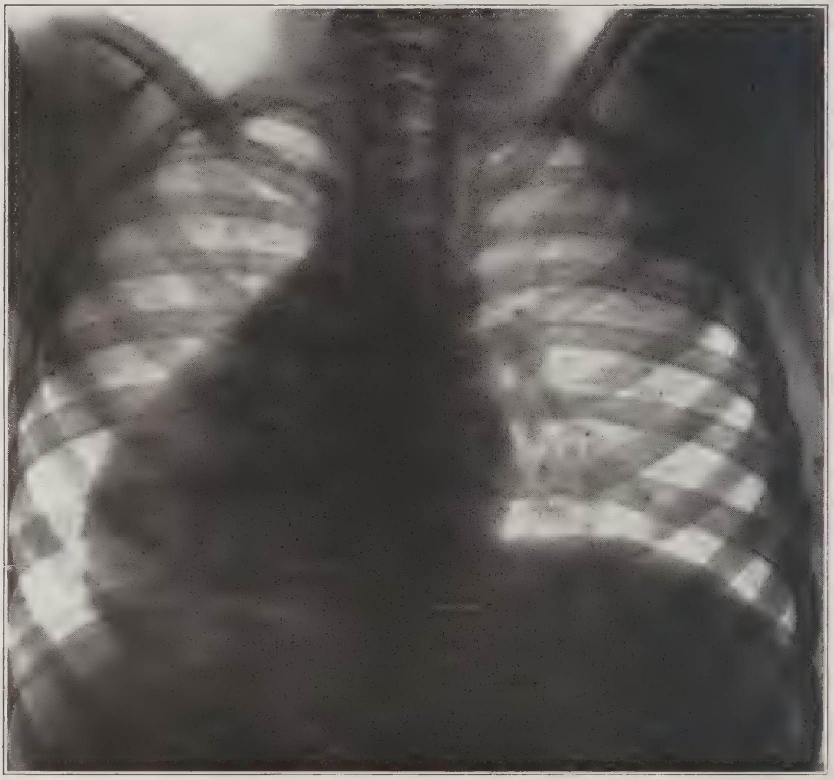

Fig. 3 (J. H.).—Five years after operation, the lungs were clear. The mediastinum was now of normal size. The heart was enlarged. The patient appeared well nourished. He had been free of any symptoms except shortness of breath. Physical examination showed a mitral insufficiency, but nothing abnormal in the lungs.

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[12] Dmockowski, Z.: Ueber secundäre Erkrankungen der Mandeln und der Talgdrüsen bei Schwindsüchtigen, Beitr. z. path. Anat. u. z. allg. Path. **10:**481, 1891.

[13] Dieulafoy, M.: Tuberculose larvée des trois amygdales, Bull. de l'Acad. de méd., Paris **33:**437, 473, 1895 (discussion by Cornil, p. 498).

inoculated animals with bits of tonsillar tissue that had been removed at operation from individuals with no clinical evidence of tuberculosis. He found that eight of the sixty-one animals so inoculated developed tuberculosis; indicating that 13 per cent. of these sixty-one patients harbored tubercle bacilli in the tonsils, but gave no clinical evidence of tuberculosis locally or elsewhere in the body. The inoculation experiments with adenoid tissue showed that 20 per cent. of the thirty-five individuals examined had tubercle bacilli in this region. This report was violently criticized by Cornil, but aroused interest in the question as to whether or not the lymphoid tissue in the pharynx is a common portal of entry in tuberculosis.

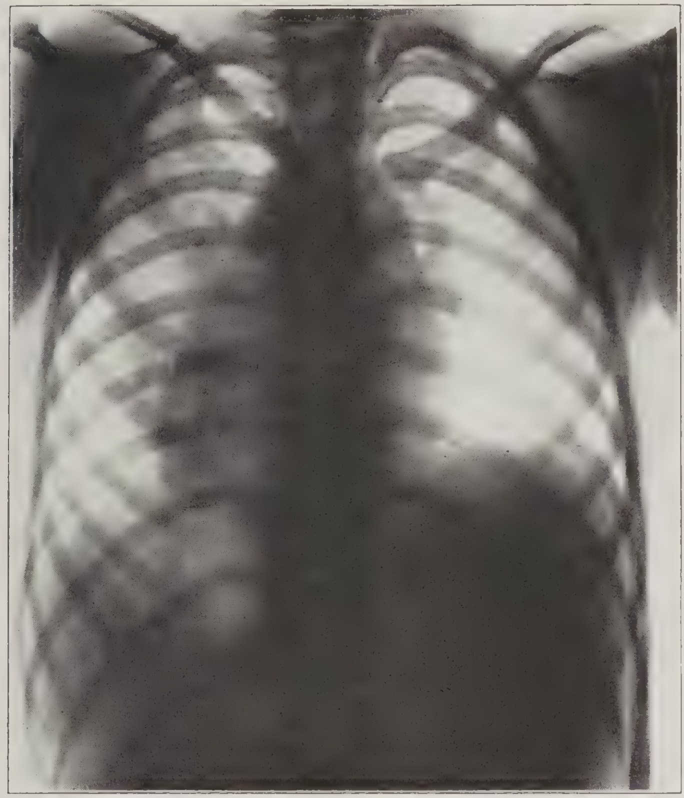

Fig. 4.—C. N., white girl, aged 7, two months after operation. The lungs were clear. The mediastinal glands were enlarged, suggesting mediastinal tuberculosis. Physical examination before operation was negative except for tuberculous cervical adenitis. Both tonsils were found to be tuberculous.

The following publications that have appeared during the past twenty years are important. Harbitz,[14] in 1905, found that cervical lymph glands removed soon after death from individuals killed in accidents often contained tubercle bacilli, virulent for animals, although no gross or microscopic evidence of tuberculosis could be demonstrated in the glands. It is his impression that organisms of all kinds are constantly passing through the lymphoid tissue in the pharynx to the cervical glands. In many instances, these organisms cause no local or general symptoms until some intercurrent infection lowers the

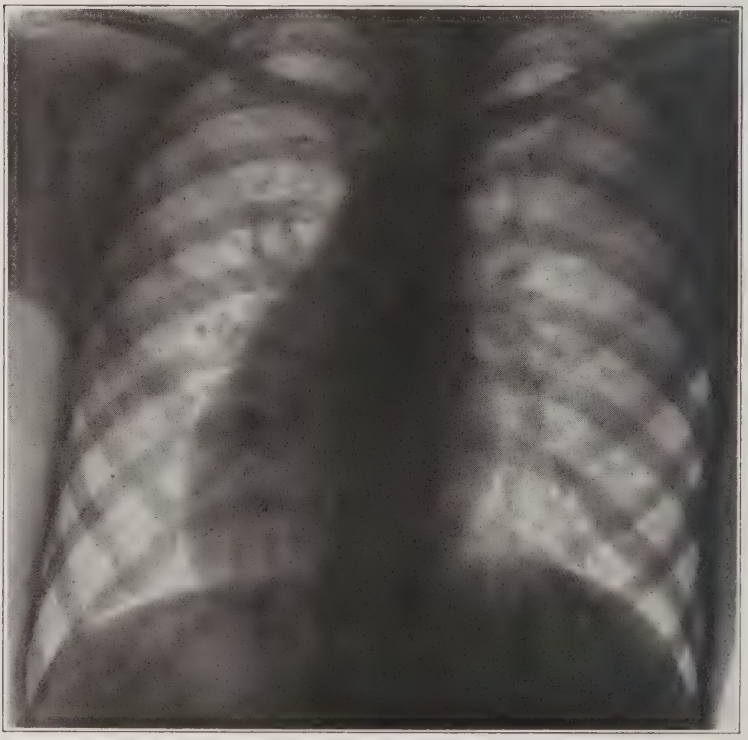

Fig. 5 (C. N.).—Four years later, the mediastinum was almost within normal limits, but there was increased root fibrosis with thickened bronchial shadows extending into the lung proper of both upper lobes. Symptoms of cough, fever and gastro-intestinal disturbances developed six months after operation. The breath sounds were harsh, but no râles were heard. The patient received tuberculin treatment and very careful general hygienic care and has had no symptoms for the past two years.

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[14] Harbitz, F.: Studies in the Frequency, Localization and Modes of Dissemination of Tuberculosis, with Special Reference to Its Occurrence in the Lymph Nodes and During Childhood, J. Infect. Dis. **2**:143, 1905.

resistance. Wood,[15] in Philadelphia, whose anatomic studies on the lymphatic drainage of the tonsils are well known, has made important contributions in regard to tuberculous and other infections of the tonsils. Wood describes lymphatics from the tonsils that lead directly to a cervical lymph gland located in the triangle between the ascending process of the mandible, the anterior border of the sternomastoid and the posterior belly of the digastric muscle. He calls this the tonsillar gland. It is usually the first of the cervical glands to enlarge when the tonsil is acutely infected; it is almost invariably enlarged in association

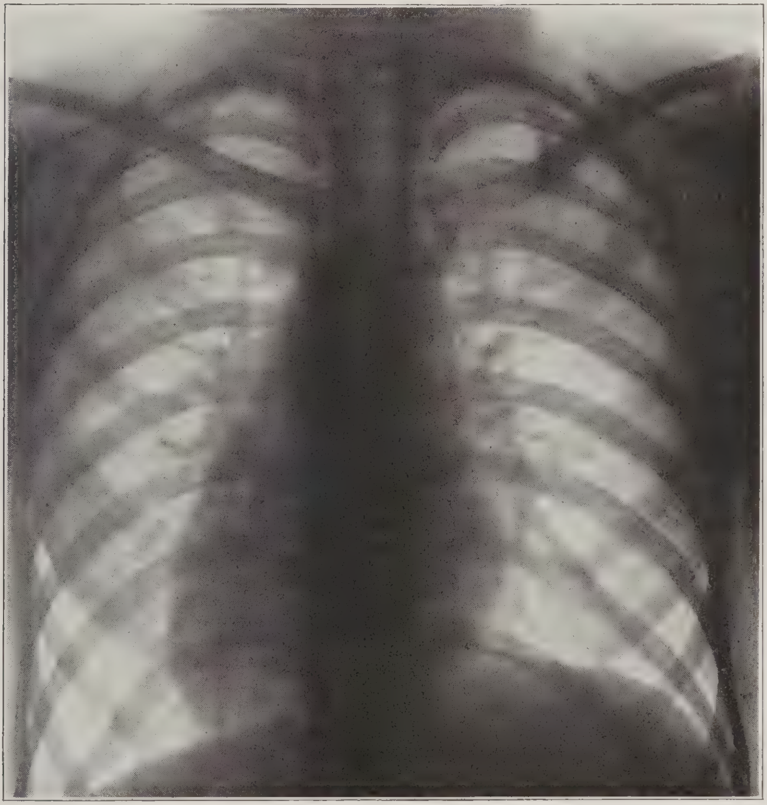

Fig. 6 (C. N.).—Seven years after operation, the mediastinum was normal. There were definite changes in both uppers beneath the clavicles, more marked on the right side. The apices were clear. The condition suggested an old fibroid tuberculosis. The percussion note was impaired and the breath sounds were roughened over both uppers. The patient has been free of symptoms for over five years, and is able to keep up her school work.

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[15] Wood, G. B.: The Significance of Tuberculous Deposits in the Tonsils, J. A. M. A. **44:**1425 (May 6) 1905; Lymphatic Drainage of the Faucial Tonsils, Am. J. M. Sc. **130:**216, 1905.

with a chronic tonsillitis, and in both tuberculous cervical adenitis and Hodgkin's disease a visible increase in size of the glands near the angle of the jaw is often the earliest evidence of the disease. Van Ree,[16] in a recent study of 205 patients with tuberculous cervical adenitis, found the oldest lesion in the tonsillar gland in 50 per cent. of the cases. Mitchell,[17] in 1914 and 1916, published several interesting papers on the frequency and the types of tubercle bacilli in the milk in England, and on primary tuberculosis of the faucial tonsils in children. He finds the bovine bacillus in 75 per cent. of the tuberculous tonsils in children

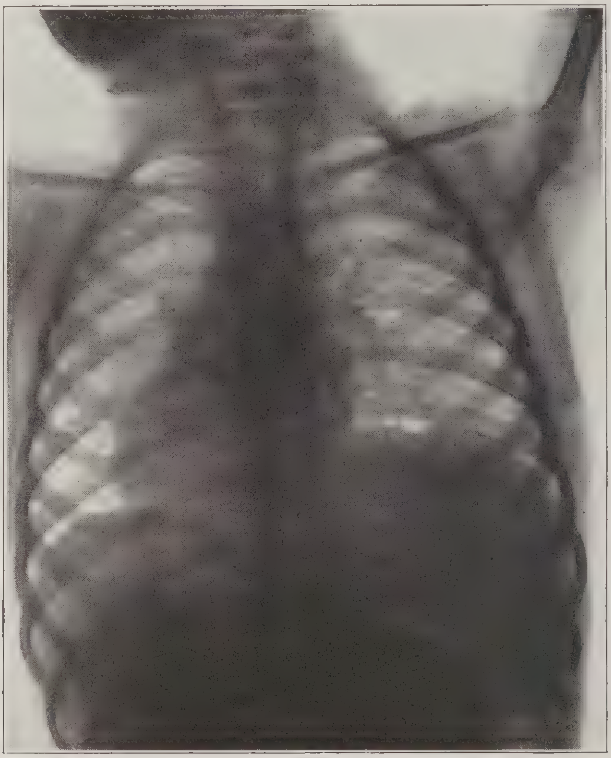

Fig. 7.—E. B., white girl, aged 3; before operation. The mediastinal glands were not enlarged. The symmetrical bilateral fibrosis indicated a nontuberculous infection. Physical examination was negative except for phlyctenular conjunctivitis and chronic tonsillitis. After operation, both tonsils and adenoids were found to be tuberculous. Tuberculous cervical adenitis developed on the left side within a month after the operation. The gland was incised.

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[16] Van Ree, A.: Die tuberkulose der amandelen, Nederl. Tijdschr. v. Geneesk. **12**:796, 1919.

[17] Mitchell, A. P.: Primary Tuberculosis of the Faucial Tonsils in Children, J. Path. & Bacteriol. **21**:248 (April) 1917; Report on the Infection of Children with the Bovine Tubercle Bacillus, Brit. M. J. **1**:125, 1914.

under 10 years of age. Park and Krumweide[18] of the New York Board of Health arrived at much the same conclusion in regard to the type of organism in tuberculous cervical adenitis in children. Only one or two cases of pulmonary tuberculosis have been reported in which the bovine bacillus was the organism responsible for the lesion, but there are numerous studies that show the frequent association of tubercles in the tonsils or adenoids and tuberculous glands of the neck.

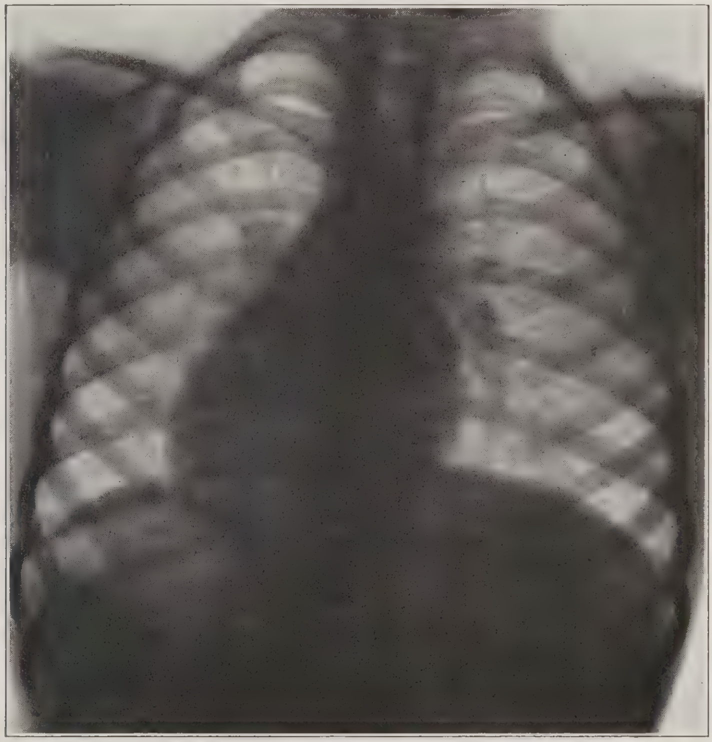

Fig. 8 (E. B.).—Three years later, the lungs were clear, the mediastinal glands slightly enlarged. The tuberculous sinus on left side of the neck healed within three months. The patient has never had any symptoms of tuberculosis and appears in good health. The physical examination was negative.

Enlarged glands of the neck are rarely seen in the sanatoriums in which advanced cases of pulmonary tuberculosis are treated.

It would seem justifiable to conclude, therefore, that in a majority of the cases of the tuberculous tonsils and cervical glands in children, the condition is primarily due to the drinking of milk from infected cows. In our series of 138 cases of tuberculosis of the tonsils or adenoids, we found a group of fifteen children in whom the adenoids alone were involved. In each of these fifteen children, repeated physical and roentgen-ray examinations have failed to disclose any evidence of tuberculosis in the cervical or mediastinal glands or in the lungs, although the tuberculin test remains positive. It is difficult to explain this apparently primary infection in the naso-pharynx on any other basis than that of an air-borne infection. Our methods, however, are subject to a large percentage of error, and no attempt was made in our series to determine the type of the tubercle bacillus, so we are unable to say definitely that the tonsils were not involved or that the organism was of the human type.

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[18] Park, W. H., and Krumweide, C.: Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis, J. Med. Research **18**:205, 1910.

Table 1.—*Summary of Finding of Various Authors*

Authors	Year	Total Number	Number Tuberculous	Percentage	Remarks
Tonsillectomy and Adenoidectomy in Patients Showing No Clinical Tuberculosis					
Friedmann	1900	53	1	1.9	
Wood	1905	50	1	2.0	
Bandilier	1906	78	1	1.3	Mostly adults
Mathews	1910	57	0	0.0	
Sewall	1911	772	30	3.9	Includes eleven patients with cervical adenitis
Barnes	1914	150	3	2.0	
Willis	1914	108	9	8.3	
Mitchell	1916	100	9	9.0	
Crowe	1917	1,000	46	4.6	Includes twenty-three patients with cervical adenitis
Van Ree	1917	92	2	2.2	Tonsillectomy only
		2,460	102	4.15	
Tonsillectomy and Adenoidectomy in Patients with Tuberculous Cervical Adenitis					
Carmichael	1910	50	7	14.0	
Mitchell	1916	106	41	38.7	
		156	48	30.76	
Adenoidectomy in Patients with No Clinical Tuberculosis					
Brindel	1896	64	8	12.5	
McBride	1897	100	3	3.0	
Luzzatti	1897	50	2	4.0	
Brieger	1898	75	5	6.7	
Lewin	1899	200	9	4.5	
Pfiffl	1899	100	3	3.0	
Wex	1899	210	7	3.4	
Rethi	1900	100	6	6.0	
Hynitsche	1900	180	7	3.9	
Lartigau	1902	75	10	13.4	
Van Ree	1919	62	7	11.3	
		1,216	67	5.5	

Table 1 presents a summary of all reports, of at least fifty cases, in which the tonsils and adenoids were removed at operation from patients with no clinical evidence of pulmonary tuberculosis.

In a previous publication, in 1917, it was pointed out that a routine histologic examination of 1,000 tonsils and adenoids removed at operation showed that forty-six of these 1,000 patients had a tuberculous infection of the tonsils or of the lymph-adenoid tissue removed from the nasopharynx. In these forty-six cases, there was an associated tuberculous cervical adenitis, confirmed by operation, in twenty-three instances. In the remaining twenty-three patients, no evidence of tuberculosis could be found on physical examination, nor did their history or general appearance suggest tuberculosis. During the four years from 1917 to 1921, a microscopic study of the tonsils or adenoids removed at operation in 2,260 additional cases resulted in the discovery of ninety-two patients with a tuberculous infection. Of these ninety-two patients, eighteen had tuberculosis of the cervical glands, but in the remaining seventy-four cases tuberculosis was not suspected until the tonsils were studied microscopically. To summarize: The histologic examination of the tonsils and adenoids removed at operation in a series of 3,260 cases resulted in the discovery of tuberculous tonsils

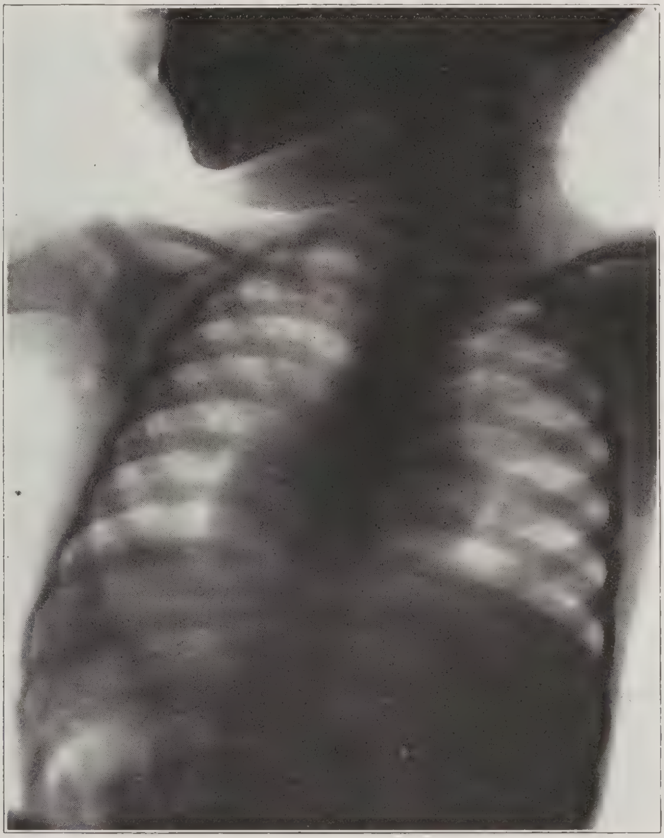

Fig. 9.—L. T., colored boy, aged 2, two years before operation. The mediastinal glands were enlarged, with beginning root infiltration, suggesting mediastinal tuberculosis. Physical examination was negative except for suppurative otitis media and phlyctenular conjunctivitis.

or adenoids in 138 patients; eighty-five of the 3,260 patients had tuberculous glands of the neck—as proved by a microscopic examination of an excised gland—but we were able to demonstrate an associated tuberculosis of the tonsils or adenoids in only forty-six of the eighty-five cases. If we deduct the forty-six cases in which tuberculous tonsils were found in association with a tuberculous cervical adenitis from the total of 138 cases of tuberculous tonsils or adenoids, we still have ninety-two in which there were no general or local manifestations of tuberculosis. Each of these patients applied for treatment on account of discharging ears, frequent colds or attacks of tonsillitis, and a tuberculous lesion was not suspected until the excised tonsils or adenoids were examined microscopically.

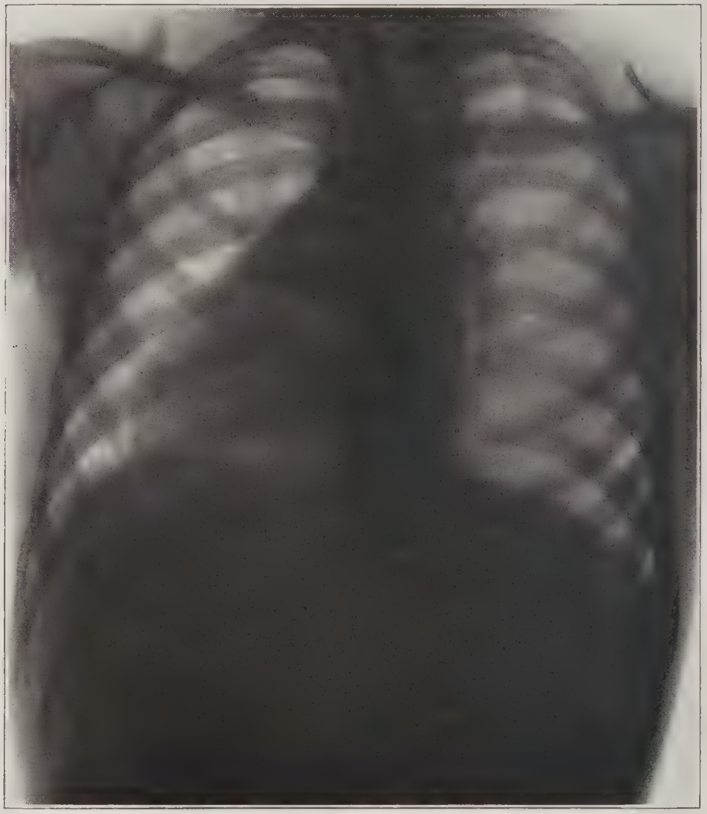

Fig. 10 (L. T.).—Five years later, the mediastinal glands were still enlarged. The infiltration had extended into the second zone of the left upper lobe. The apices above the clavicles were clear. Examination of the lungs was negative. Adenoids were found to be tuberculous; the tonsils were not tuberculous. There was no tuberculous cervical adenitis and no conjunctivitis.

It is desirable to know the ultimate result in these patients with an apparently primary tuberculosis of the lymph-adenoid tissue in the throat. Will they subsequently develop clinical evidence of tuberculosis in the cervical or mediastinal glands, in the lungs, or elsewhere in the body? When tubercles are discovered in the tonsil by histologic examination and no clinical manifestations of the disease are evident on physical examination, should we notify the parents of the child, or the patient himself if he is an adult? Is it necessary to withdraw the child from school, or send the adult to a sanatorium in order to improve the general physical condition and to educate the patient to conform to the rules for the recovery from tuberculosis? Does the discovery, through histologic examination, of tubercles in the tonsils or adenoids

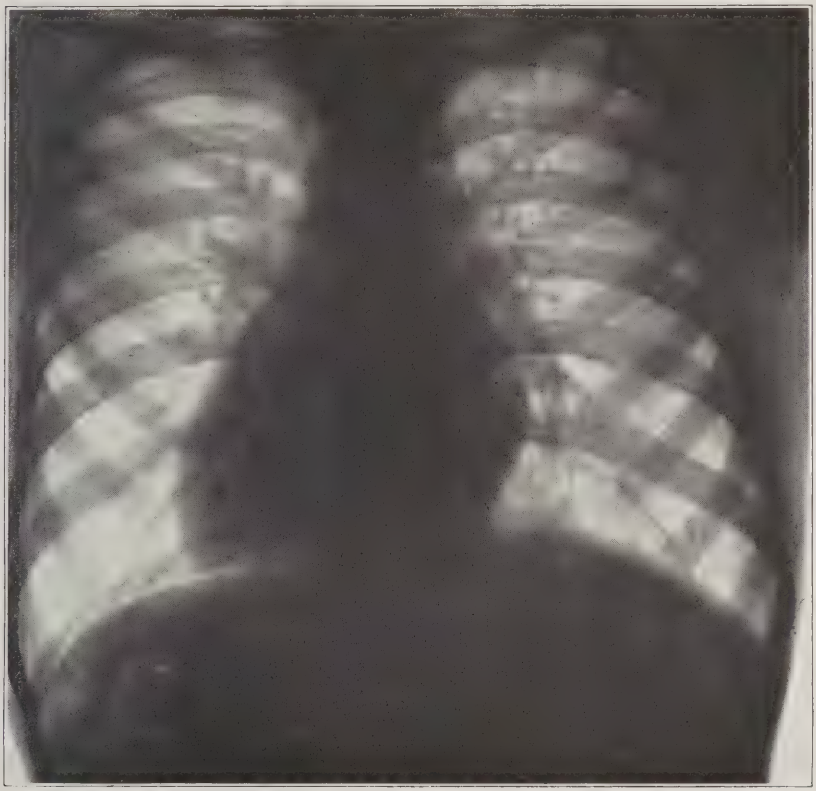

Fig. 11 (L. T.).—Two years later, the mediastinum was within normal limits. There were numerous small calcified glands in the root zone extending into the second zone. The apices above the clavicles were cloudy. The roentgen-ray impression is fibroid tuberculosis of both uppers. The lungs showed impairment of the percussion note over both upper lobes, but no changes in the breath sounds. The general health was good. The ears were normal.

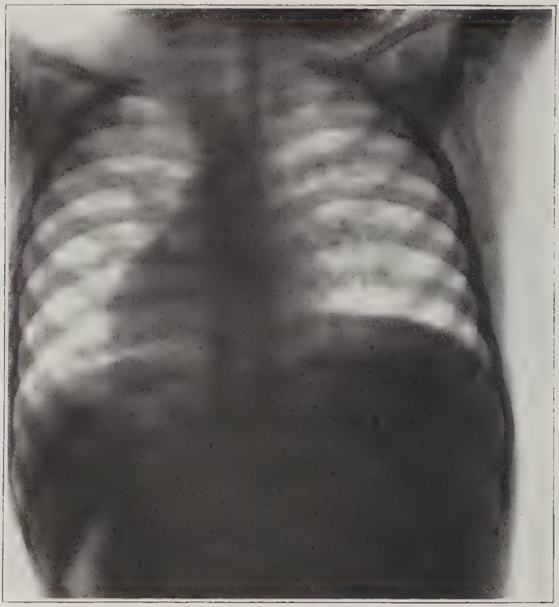

Fig. 12.—I. S., colored girl, aged 1½; before operation. The mediastinum was not enlarged. There was slight infiltration of the left upper lobe extending beyond the root zone, strongly suggestive of pulmonary tuberculosis. The lungs were clear on physical examination. There was tuberculous cervical adenitis on the left side. After the operation, the adenoids were found to be tuberculous; the tonsils were not tuberculous.

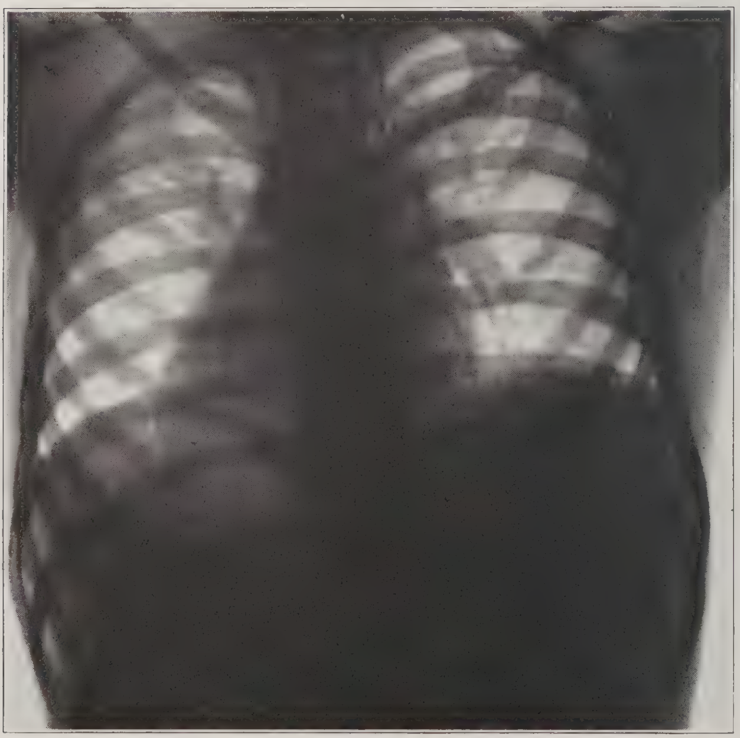

Fig. 13 (I. S.).—Five years later, the mediastinum was enlarged, with fibrosis of both upper lobes, especially the left, tuberculous in origin. A recent physical examination was negative. The cervical adenitis subsided shortly after operation. The patient appears healthy and robust.

indicate that there is already a widespread distribution of tubercle bacilli, or can we assume that the infection is local, and since it produces no local symptoms, is of no significance and may be ignored?

These are pertinent questions that any physician may be called on to answer. Our patients include physicians, nurses, students and children that have always received the best of care, as well as those from the class that visit the outpatient department of the hospital. In order to answer these questions, it will be necessary to observe a group of such patients for ten or fifteen years, with frequent physical examinations and a roentgen ray of the lungs at least once each year.

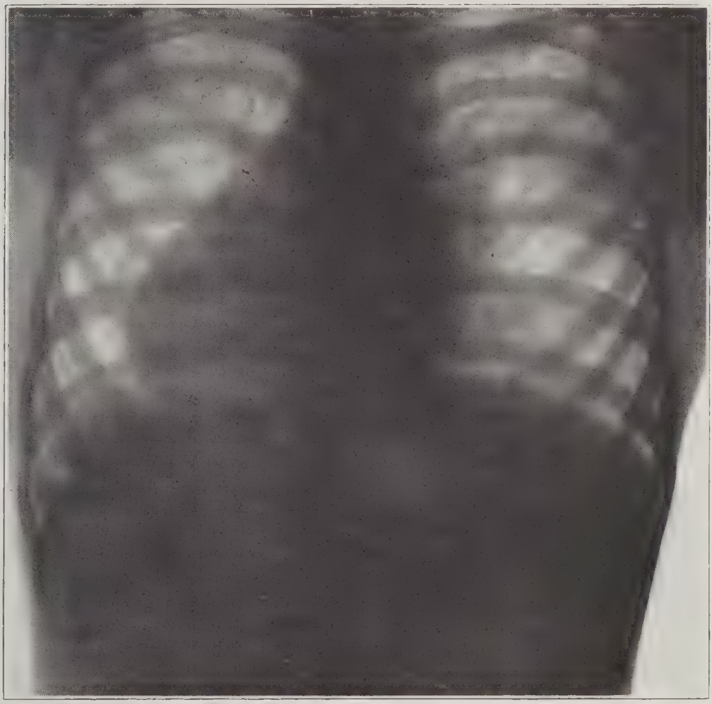

Fig. 14.— J. H., colored girl, aged 6; before operation. The mediastinal shadow was slightly enlarged. The apices were clear. The soft infiltration beneath both clavicles suggested an active tuberculosis. The patient had had no symptoms except tonsillitis. Physical examination of the lungs showed a few sonorous râles along the inner border of both scapulae, but pulmonary tuberculosis was not diagnosed. The adenoids were found to be tuberculous, but the tonsils were not.

It is difficult to persuade patients that are free from clinical symptoms to return year after year for observation, but with the aid of the social service department, the Phipps department for the study of tuberculosis, the staff of the Harriet Lane Home for children, and the special fund for the study of tuberculosis in the Johns Hopkins Hospital, we have been able to obtain accurate records, and a total of 100 roentgenograms of the lungs on fifty of our cases from the outpatient department. Each of these fifty patients had tubercles in either the tonsils or the adenoids, as shown by histologic examination; forty have been under observation for five years or longer, and in the remaining ten cases, at least two years has elapsed since the operation.

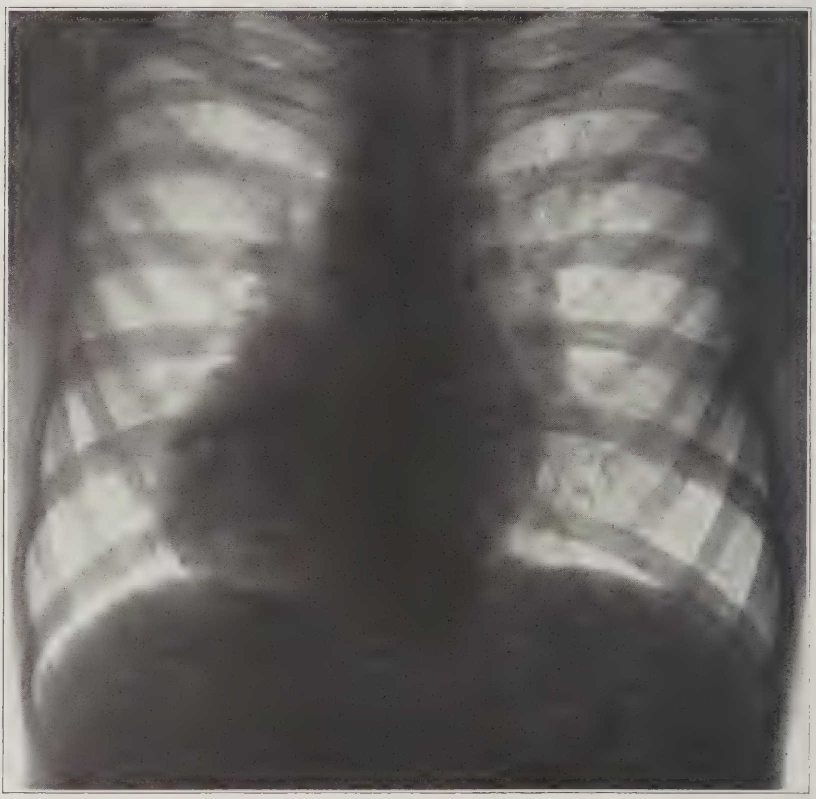

Fig. 15 (J. H.).—Five years later, both upper lobes showed decided fibrosis, suggesting end-result of tuberculosis. Repeated physical examinations during the period of observation showed no evidence of active pulmonary tuberculosis. The general health is good. The patient appears healthy and robust.

In addition to the questions enumerated above, these fifty cases have been studied in order to determine the following points:

1. Is there any roentgen-ray evidence of tuberculosis in the lungs or the mediastinal glands? And if suspicious lesions are found, do they progress or retrogress during a five-year period of observation?

2. Has the use of ether anesthesia been detrimental?

3. Do the children that had a positive tuberculin test at the time of their first examination, prior to operation, and in whom tuberculous tonsils or adenoids were found when the excised tissues were examined histologically, have a negative reaction at any time subsequent to the operation?

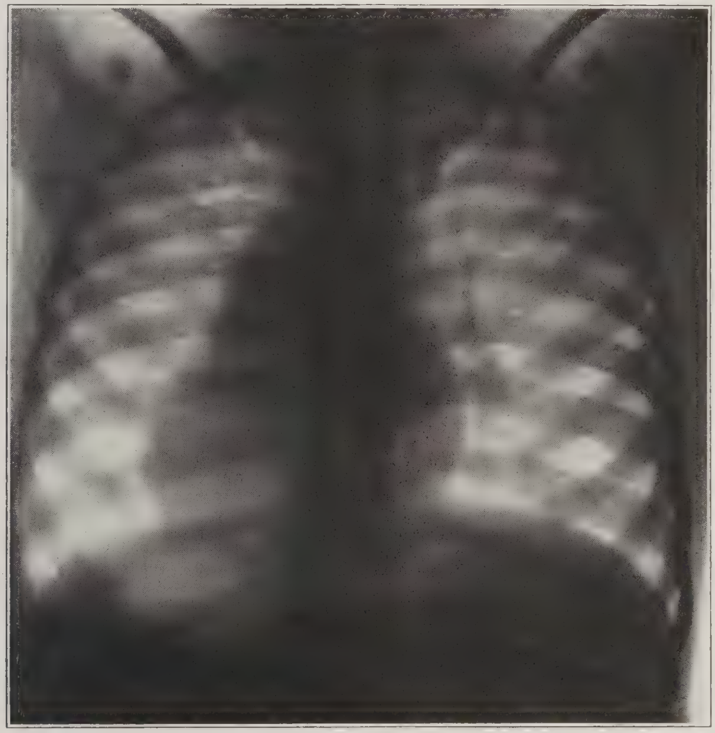

Fig. 16.—R. B., colored boy, aged 5. One year after operation. The mediastinal glands were enlarged, suggesting mediastinal tuberculosis. Physical examinations at the time the roentgenograms were made and before operation were negative except for a tuberculous cervical adenitis on the right side. Only the right tonsil was found to be tuberculous.

SUMMARY OF POSTOPERATIVE OBSERVATIONS

Following is a brief summary of the information we have acquired from the postoperative observation of the fifty cases mentioned above:

Tuberculosis of the Cervical Lymph Glands. — This condition developed in only two patients during the postoperative period of observation. One was a white woman, aged 27, who first came to the outpatient department in 1914, complaining of frequent attacks of tonsillitis. Tuberculosis was not suspected until the microscopic sections of the tonsils were studied. This patient has had numerous physical examinations and roentgen-ray examinations of the chest during the nine years since her tonsillectomy, but no evidence of tuberculosis was discovered until the glands at the angle of the jaw on the right began to enlarge, eighteen months after the operation. The tuberculous glands were removed, and she is now apparently perfectly well. No clinical or roentgen-ray evidence of tuberculosis of the lungs has ever been discovered.

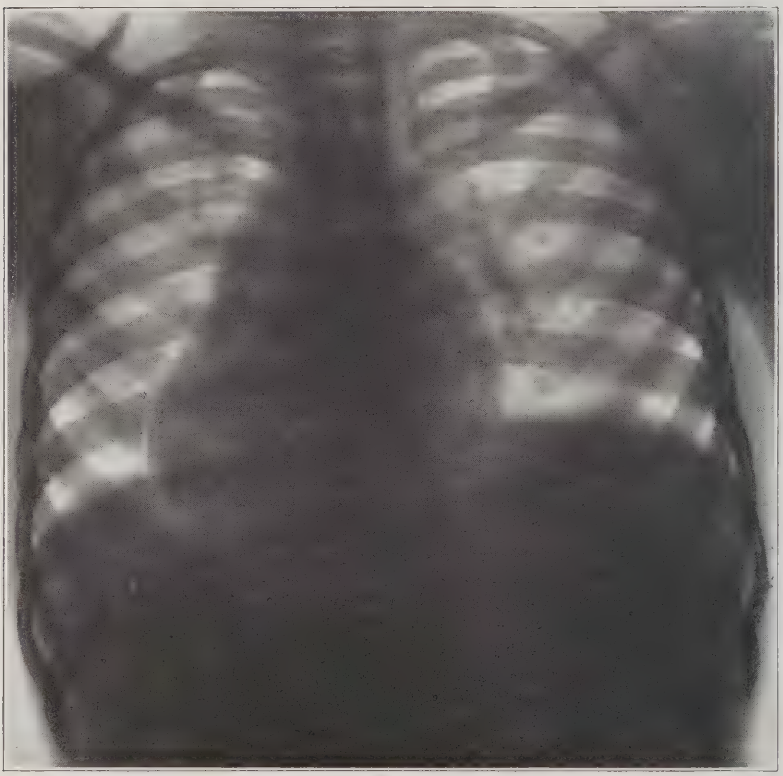

Fig. 17 (R. B.).—Three and one half years after operation, the lungs were clear. The mediastinal glands were large and tuberculous. The cervical glands on the right were excised two years ago. No further symptoms developed. The general health is good and a recent physical examination was negative.

The other patient that developed tuberculous cervical adenitis during the postoperative period of observation was a white child, aged 3 years, who was brought to the outpatient department, in 1919, with phlyctenular conjunctivitis. The father had died of tuberculosis in 1918. The tonsils and adenoids were removed, and on microscopic examination, tubercles were found in each of the tonsils and in the adenoid tissue. Tuberculous glands appeared on the left side of the neck three months after operation; they were incised and curetted, and have gradually disappeared. At present, over four years after the tonsillectomy, this child is apparently in perfect health.

Tuberculosis of the Mediastinal Lymph Glands.—This condition has been diagnosed in our series from the roentgenogram of the chest. In three children, the roentgenogram made before operation showed a normal mediastinum. The tonsils were removed, and were found to be tuberculous, and subsequent roentgenograms showed enlarged mediastinal glands. Each of these children was under the observation of the pediatric department, and the home conditions were improved by visiting nurses. In a colored child, first seen at the age of 1½ years, the enlarged mediastinal glands were first noticed 5 years after the discovery of the tuberculous infection in the tonsils. In a white child, first seen at the age of 3 years, the enlarged mediastinal glands were

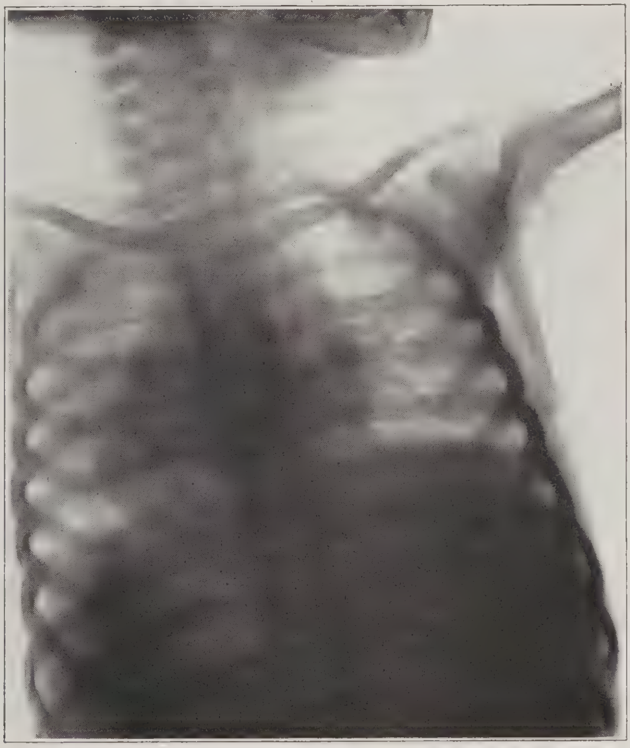

Fig. 18.—G. C., colored girl, aged 4. One year before operation. The enlargement of the mediastinal glands with fibrosis at the left apex were tuberculous in origin. Two years before operation, the child developed scattered tuberculids following an incision of a tuberculous gland in the right side of the neck. The tuberculids disappeared before operation. Only the right tonsil was tuberculous. Repeated physical examinations of the lungs were entirely negative.

first noticed three years after operation. The remaining patient, a white child, aged 6 years, had no roentgen-ray or clinical evidence of a mediastinal lesion before operation, but a roentgenogram taken six months later showed definitely enlarged mediastinal glands. A roentgenogram made five years after operation showed that the enlarged glands had subsided and the mediastinum was again normal. These three children have grown and developed normally, go to a public school and are apparently perfectly well.

Tuberculosis of the Lungs.—During the postoperative period of observation, pulmonary tuberculosis developed in five patients—three children and two adults. In only one, a child, aged 7 years, is there any clinical symptom of the lesion in the lung that was diagnosed from the roentgenogram as pulmonary tuberculosis. In the remaining four patients, the roentgen-ray changes in the lungs that were first noted two years after operation gradually became fibroid in character.

No one of the four other patients mentioned above ever had fever, cough, loss of weight, anorexia or any other of the common symptoms of pulmonary tuberculosis. The one child that had both roentgen-ray and clinical evidence of a pulmonary lesion is apparently cured. For several years, she was an inmate of an open-air school, but she has now returned to the city and goes to a public school.

Tuberculosis of the Bones and Joints.—This condition appeared in two patients, one an adult and one a child. In each case, tuberculous tonsils or adenoids had been removed from one and one half to four and one half years before the onset of the joint symptoms. A white man, aged 22 years, had his tonsils and adenoids removed in 1917, on account of a tuberculous cervical adenitis. Microscopic sections showed tubercles in both of the tonsils, in the adenoids and in the excised glands. A psoas abscess and a tuberculous lesion in the third lumbar vertebra appeared one and one half years after tonsillectomy. Drainage of the abscess and an Albee graft by Dr. W. S. Baer have resulted in an apparent cure. In a white child, aged 2 years, the adenoids alone were removed on account of a chronic suppurative otitis media. The ear condition rapidly healed. Symptoms of tuberculosis of the hip first appeared four and one half years after the adenoidectomy. The child was greatly improved by fixation and traction of the affected leg, and there is no clinical evidence of tuberculosis elsewhere in the body.

Cervical Adenitis Group.—A roentgen-ray diagnosis of tuberculosis of the mediastinum or lungs was made in thirteen out of a group of eighteen patients in whom the tonsils and adenoids were removed because of a definite tuberculous cervical adenitis. In the remaining five patients, repeated physical and roentgen-ray examinations, over a period of five years, have revealed no involvement of either the medi-

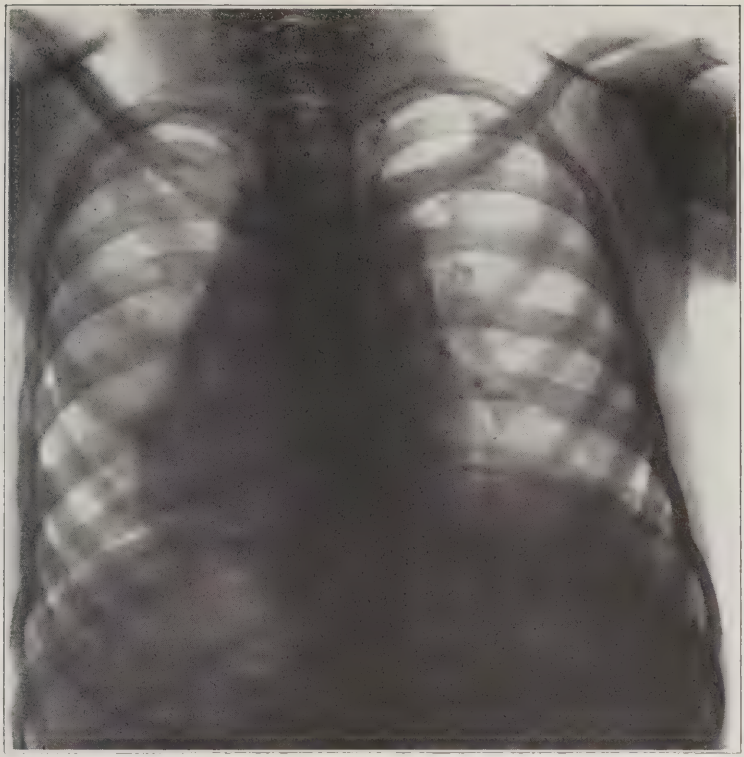

Fig. 19 (G. C.).—Four years later, the large mediastinal glands with fibrosis at the left apex were still noted. The cervical glands were still visibly enlarged, but they have caused no symptoms for past two years. The patient's health is good. A recent physical examination of the lungs was negative.

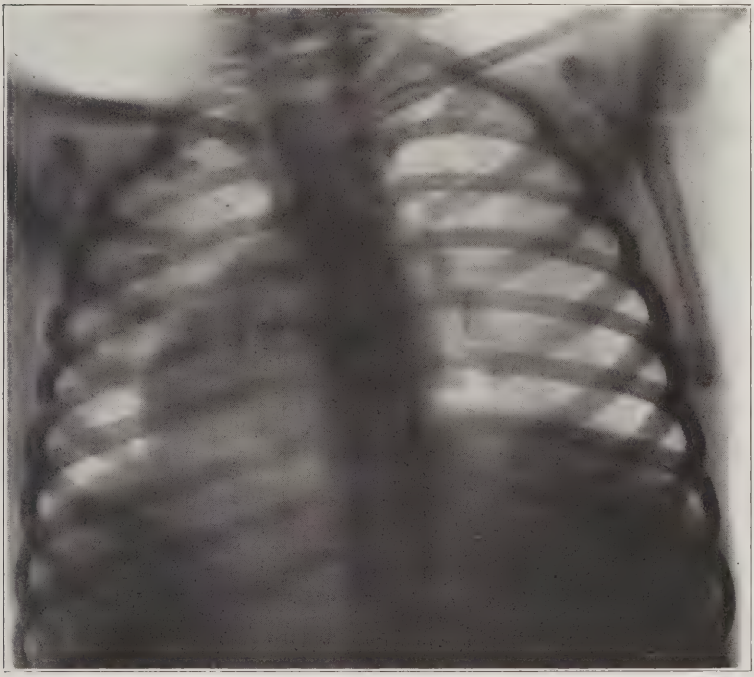

Fig. 20.—N. N., colored boy, aged 6, two years after operation. The mediastinal glands were slightly enlarged, suggesting a mediastinal tuberculosis. The lungs were clear except for occasional scattered râles. The patient had been under constant observation since 1 year of age, for chronic bronchitis. After operation, both tonsils were found to be tuberculous.

astinum or the lungs. In five of the thirteen patients having cervical adenitis, with mediastinal or lung involvement, a series of roentgenograms show a progression of the lesion during the five year period following the removal of the tuberculous tonsils. Only two of these five patients developed clinical symptoms. One is dead, and the other is now free from symptoms. In three of the thirteen cases mentioned above, tuberculous lesions appeared in the roentgenograms made during the period of postoperative observation. In one, enlarged mediastinal glands, with no evidence of a pulmonary lesion, was first noted three years after tonsillectomy. In one, the roentgenogram made before operation revealed a slight fibrosis in the lung, but enlargement of the mediastinal glands was first noted five years later. There have been no clinical symptoms referable to the lungs in either of these patients. In all of the patients mentioned in this paragraph, the indication for tonsillectomy was an evident tuberculous cervical adenitis, and in each of these eighteen cases, the tonsils were proved tuberculous by histologic examination.

Summary of Roentgen-Ray Examinations.—Our data in regard to the involvement of the mediastinum or lungs in the group in which no tuberculosis was suspected at the time of the tonsillectomy is based on a clinical and roentgen-ray study of twenty-two cases. In ten patients, no roentgen-ray or clinical evidence of a mediastinal or lung lesion has been found during the five years of postoperative observation. In six patients, the enlargement of the mediastinal glands or the roentgen-ray evidence of a lung lesion, shown in roentgenograms taken soon after the tonsillectomy, has entirely disappeared; while in the remaining six patients, the lesions in the chest have progressed according to the roentgenograms, but no one of these six has had fever, cough, râles or other evidence of a clinical tuberculosis.

Summary of Incidence in the Johns Hopkins Hospital.—The general incidence of tuberculosis of the tonsils and adenoids as noted in the literature approximates 5 per cent.; while in patients with manifest tuberculous cervical adenitis, the incidence varies from 20 to 72 per cent., depending on the technic. In this series, the general incidence is 4.18 per cent., while it rose to 48.2 per cent. in the patients with tuberculous cervical adenitis. Among patients with no clinical evidence of tuberculosis, it falls below 2 per cent. Although not shown in Table 2, tuberculosis of the tonsils and adenoids occurred four times as frequently in the colored as in the white race.

It can be seen from Table 3 that more than half of the tuberculous patients were under 10 years of age. These figures stand in marked contrast to those of Weller, who found the greatest incidence in young adults. Might not this increase in the incidence among very young children tend to connect tuberculosis of the tonsils and adenoids with the primary tuberculous infection of childhood rather than with the clinical tuberculosis of young adults?

The use of ether anesthesia for the removal of tonsils and adenoids has been most satisfactory in our experience, and we see no reason why we should substitute gas and oxygen or a local anesthetic. With the exception of a few cases in which a cardiac, renal or pulmonary condition contraindicated the use of a general anesthetic, we have employed ether in all of the 3,260 cases mentioned in the early part of this paper. We do not know of a single case of postoperative lung abscess in this series of 3,260 patients; and the hospital records show only three cases of postoperative pneumonia, with recovery in each instance within ten days. Finally, the records that are summarized above of the fifty patients with a tuberculous infection and the post-operative condition of the remaining eighty-eight patients with tuberculous tonsils or adenoids that are not included in this paper, indicate that a latent tuberculous infection of the tonsils, adenoids or cervical or mediastinal glands is no contraindication to the use of ether anesthesia. We wish to emphasize the fact, however, that the anesthetic is always administered by a professional anesthetist. After the mouth gag is introduced, ether is never given in an amount sufficient to abolish the swallowing reflex, and the greatest care is taken to prevent the aspiration of blood, vomitus or bits of tissue.

TABLE 2.—*General Incidence of Tuberculosis of Tonsils and Adenoids*

Symptoms	Operation	Number of Patients	Tuberculous Lesions		Percentage
No clinical tuberculosis..........	Tonsillectomy and adenoidectomy	2,215	Tonsils or adenoids	72	3.25
No clinical tuberculosis..........	Adenoidectomy	1,000	Adenoids	25	2.5
Tuberculous cervical adenitis....	Tonsillectomy and adenoidectomy	85	Tonsils or adenoids	41	48.2
Total..................................		3,300		138	4.18

TABLE 3.—*Age Incidence*

	Tonsillectomy and Adenoidectomy		Adenoidectomy	
Years	Number	Percentage	Number	Percentage
1 to 10..............................	60	6.52	19	3.92
10 to 20..............................	32	4.7	5	2.3
Over 20..............................	21	3.0	1	1.1
Total............................	113	4.91	25	2.5

We are indebted to Dr. F. H. Baetjer, who interpreted the roentgenograms. The entire group of 100, some dating back ten years, was assembled in May, 1923, and Dr. Baetjer dictated his impression without any knowledge of the clinical condition of the patient. We are also indebted to Dr. R. J. Dunn of Sumter, S. C., who assisted in assembling the records and microscopic sections.

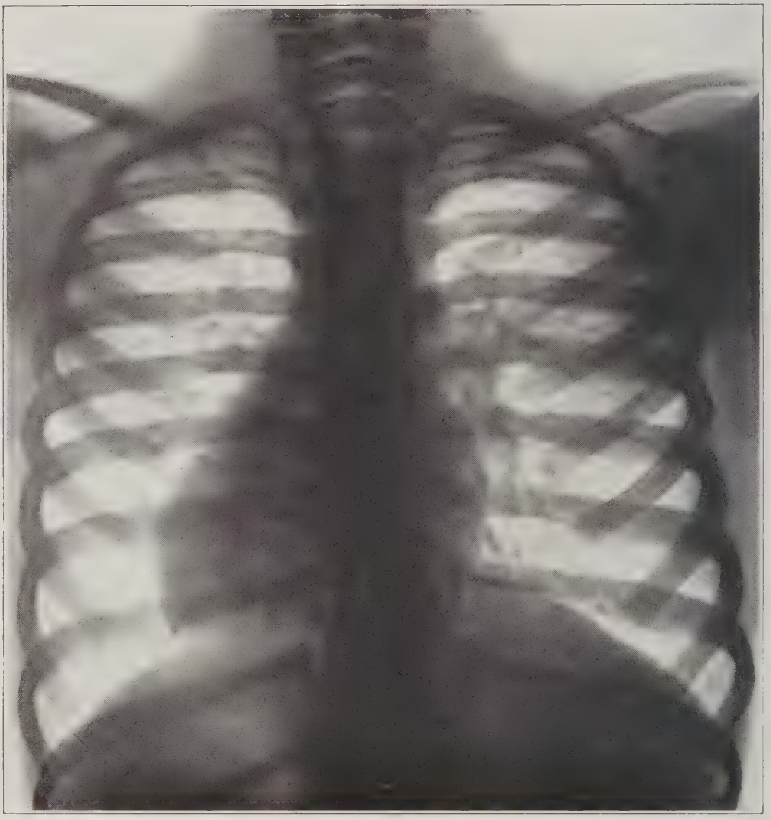

Fig. 21 (N. N.).—Three years later, the lungs were clear. The mediastinal glands at the root of the right hilum were calcified, indicating a healed process. The general health has been good. The patient showed no signs of pulmonary tuberculosis during the period of observation.

If the roentgen-ray changes in the lungs and mediastinal glands are sufficient to establish a diagnosis of tuberculous infection when the patient himself is free from all signs and symptoms of such an infection, then three-fifths of the fifty patients studied in this series had tuberculosis elsewhere in the body prior to the discovery of the lesion in the tonsils or adenoids. Our impression, based on the postoperative clinical study of this group for five years or longer, is that a tuberculous infection of the tonsils and adenoids is of but little significance and might be best ignored. It is true that a continued observation of this group for another five or ten years might result in finding an abnormally high percentage of clinical tuberculosis, but our results up to the present lead us to doubt the wisdom of notifying the patient or the family that the tonsils or adenoids, on histologic examination, show tubercles, and thus stigmatize the patient as tuberculous. In the past, we have always made such notifications, and in many instances have thus caused an unnecessary loss of time from work or study; an expenditure of funds that could be ill-spared; a large amount of mental worry to the patient, family and friends, and finally; a blot on the record if life insurance is applied for at some later date.

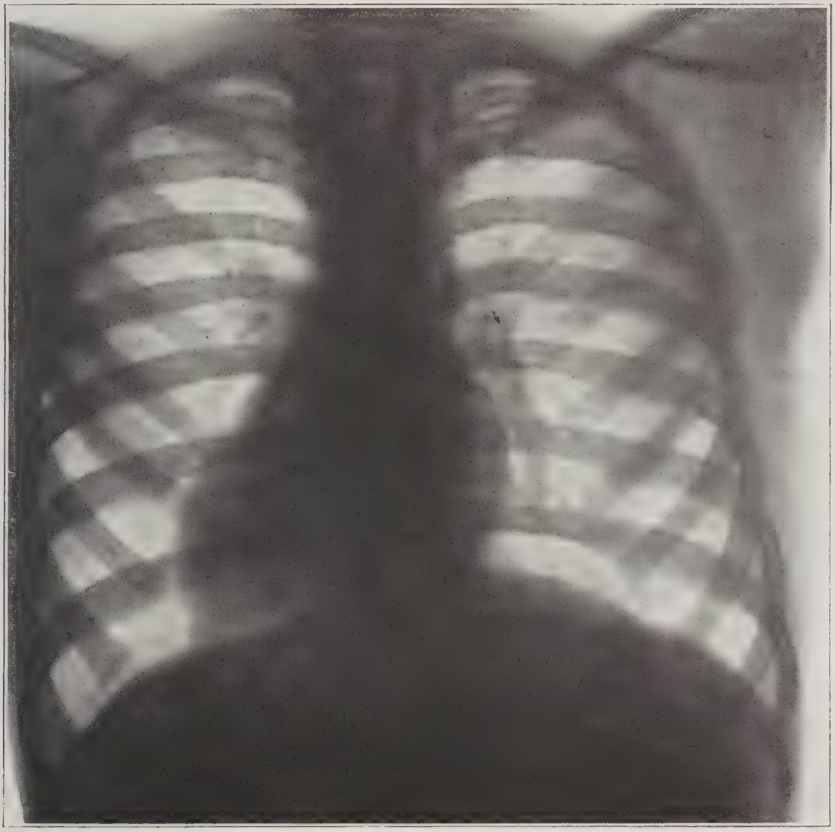

Fig. 22 (N. N.).—Eight years after operation, the mediastinum was normal. There was absorption of the root shadows. The calcified glands at the root of the right hilum were still present. The patient was in the hospital with typhoid fever. Nothing to suggest tuberculosis was found in the examination. At present the patient appears healthy and robust.

CONCLUSIONS

We have succeeded in obtaining a series of postoperative observations on fifty patients from the outpatient department of the Johns Hopkins Hospital. Forty have been observed from five to ten years, and ten for at least two years. Each of these patients has had a roentgen-ray examination of the chest and a general physical examination at least once a year since removal of the tonsils and adenoids. In each of these patients, the tuberculous lesion in the tonsil or adenoid tissue was verified by the pathologic department.

It is our impression that:

1. Tuberculosis of the tonsil is usually a bovine bacillus infection. We base this conclusion on the age incidence (over 50 per cent. of our patients were less than 10 years of age); the frequency of the involvement of the cervical and mediastinal lymph glands; the strikingly low incidence of pulmonary, intestinal or other complications during the five to ten year period of postoperative observation, and the growth, appearance and excellent general physical condition of these children in spite of the roentgen-ray evidence of tuberculosis of the mediastinum. It is possible that such a tuberculous infection of the lymph-adenoid tissue in the throat, if not complicated with frequent secondary infection, is of value from the point of view of immunity.

2. When tubercles are found in the tonsil on histologic examination, it is needless to become unduly excited, because the infection is already widespread in the cervical, mediastinal and probably the mesenteric lymph glands.

3. In such cases, the removal of tonsils and adenoids is of value in that it reduces the secondary infection, but there is no evidence that by operation on the throat one can remove the only tuberculous focus in the body.

4. Tuberculosis of the tonsils or adenoids is never recognizable from the gross appearance before operation unless there are superficial ulcerations secondary to an open pulmonary lesion; and when the lesion is discovered microscopically, it is probably not advisable to alarm the family, stigmatize the patient as tuberculous or seriously interfere with his ordinary routine duties, since the majority of such patients will probably never have clinical symptoms of the disease.[20]

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[20] Because of lack of space, a number of references in the form of a bibliography have been omitted. These are included in the reprints, a copy of which can be had on application to the author.

BLINDNESS AND OTHER DISEASES IN CHILDREN ARISING FROM DEFICIENT NUTRITION (LACK OF FAT-SOLUBLE A FACTOR)*

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While blindness in children has been on the decrease in the greater part of the civilized world, the opposite is true in Denmark. Blindness in children has increased not only absolutely but also relatively to the population. Many causes have contributed to the diminution of blindness in other countries, but the chief one undoubtedly is that gonorrheal ophthalmoblenorrhea in the new-born has become a rare disease as a result of the special measures which have been adopted against it everywhere. That gonorrheal ophthalmia has become a rarity is also true in Denmark, but in spite of this the percentage of blindness in children is increasing.

There is, however, another disease of the eye peculiar to childhood which leads to blindness: xerophthalmia. It was first described in the middle of the last century by German ophthalmologists. According to all previous reports, xerophthalmia had a serious prognosis, as it occurred particularly in the final stage of a cachectic condition due to a protracted wasting disease such as tuberculosis, syphilis, typhoid fever and acute or chronic digestive disease, and especially in badly nourished and debilitated children.

In the middle and at the close of the last century and in the beginning of this, "epidemics" of an eye disease were described which were undoubtedly identical with xerophthalmia. These epidemics occurred among negro children in Brazil, during periods of fasting in Russia and when famine and summer diarrhea appeared together in Japan, and it was always the badly nourished and diseased children of the poorer classes who were attacked. The majority of the authors who have described these epidemics therefore associate xerophthalmia in children with a poorly selected and deficient diet. Primitive medicine in Japan, Russia and other countries has from ancient times treated this eye disease with fat substances, especially cod liver oil and liver, and Mori has declared that the disease is due to lack of fat in the diet.

In Europe, xerophthalmia is considered extremely rare. A few cases have been recorded in badly nourished children in England and Denmark, while in Germany Czerny and Keller, and, according to them,

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* Received for publication, Nov. 21, 1923.

several others, have now and again observed xerophthalmia in the final stage of the nutritional disease they call "Mehlnährschaden."

The children's department of the Danish State Hospital was opened in 1911. By the next spring a number of children had been admitted with a curious eye disease which proved to be xerophthalmia, and in the following year the number increased to an alarming extent. I thus had the opportunity of studying this disease in its different forms and stages, about which I published communications in 1914, 1916, 1917, 1918 and 1922.

My investigations indicated that the disease was due to a lack of a particular substance. This substance was present in fresh milk, but not in separated milk or in buttermilk. It was therefore united with the butter fat, and it was also found in abundant quantities in cod liver oil. My investigations further showed that the disease could not be attributed to the absence of fat as such, because even though the children had received margarin or pork fat, they could easily contract xerophthalmia.

In England and the United States, a large number of experimental investigations on nutrition were carried out, partly before and partly at the same time as my work. From these inquiries, we became further acquainted with the cause of xerophthalmia and the disease associated with it. It was from the animal experiments of Osborne and Mendel, and especially of McCollum and his collaborators, that we now know the cause of xerophthalmia to be the lack of the fat-soluble A vitamin. This factor, which is united with certain fat substances and is notably found in large quantities in butter and cod liver oil, must be constantly supplied to the organism, particularly the growing organism, in order that growth shall take place. Deprivation for a long period leads to xerophthalmia and death.

When a child, particularly one in the first few years of life, is deprived of its mother's milk or fresh milk, as well as cream and butter, and is kept for a long time on a diet consisting of puddings made with separated or buttermilk, bread and other farinaceous foods, mashed potato, a little pork and other meat, margarin and pork fat, it will become ill as a result of the absence of the fat-soluble A factor. Even the consumption of a little vegetable, fruit, and green stuff now and then, will not help much, for a small child can digest only trifling amounts of green stuff.

A deficiency of the fat-soluble A factor may also occur in children who have received a quantity of pure milk that is stale and modified adversely, the fat-soluble A factor being destroyed by oxidation and repeated heating.

The disease is ushered in by failure to gain weight. Later on, there is a loss of weight and the child is quiet and apathetic. In other words, there is inhibition of growth and depressed psychic and bodily vitality.

These children are liable to be attacked by some infectious disease, which usually takes the form of a simple catarrhal infection of the mucous membranes, particularly of the respiratory organs and middle ear. *B. coli* infections of the urinary tract and infectious dermatitis are also frequently observed. These infections are extraordinarily persistent and often have a fatal issue. An increased susceptibility and a diminished power of resistance to infections are therefore present.

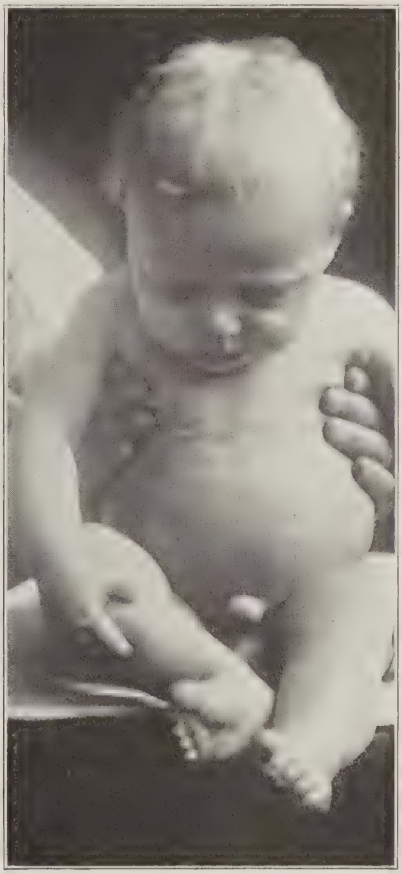

Fig. 1.—Child with xerophthalmia.

The eye lesion does not appear as a rule until late in the disease. The first symptom is night-blindness (hemeralopia) and dryness of the ocular conjunctiva (xerosis). The dryness later extends over the cornea, which becomes hazy, shrivels up, and shortly after, pieces of it become necrosed (keratomalacia). In most cases, the ocular conjunctiva is infected; the child then has photophobia; the conjunctiva is red and swollen, and the eyes begin to water. When the cornea necroses, the inflammation spreads to the interior of the eye. The inflammation may be so intense and widespread in many cases that it almost obscures the original xerosis. The eye lesion can with difficulty be distinguished from the destructive inflammation in such cases.

If the disease is not recognized in time, the child becomes blind. If the child does not then die of a secondary infection, the most frequent cause of death is bronchopneumonia.

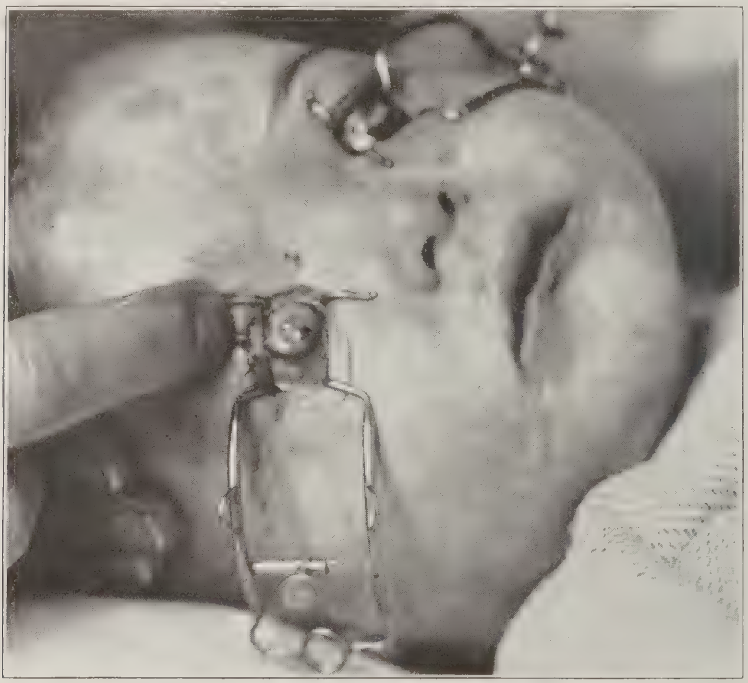

Fig. 2.—Child with xerophthalmia, showing eye lesion.

A boy (Fig. 1), aged about 2 years, appeared to be a healthy child, except that the eyes were swollen and kept tightly closed. He was small and under weight, and had a catarrhal infection. His eyes were completely destroyed by the disease, as is shown in Fig. 2. The conjunctiva was swollen and red, both corneas were necrotic and there was pus in the anterior chamber. The child was cured, but became totally blind, as the cornea never heals with clear transparent tissue.

The scars are always hazy and opaque, as will be observed from the succeeding pictures of children who were cured (Figs. 3 and 4). In cases in which the cornea is only partly damaged, the child can usually be saved from complete blindness.

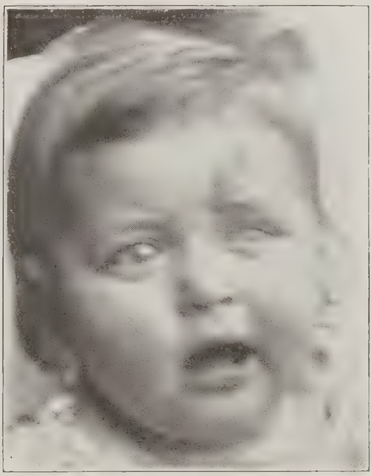

Fig. 3.—Recovery from xerophthalmia, showing permanent eye location.

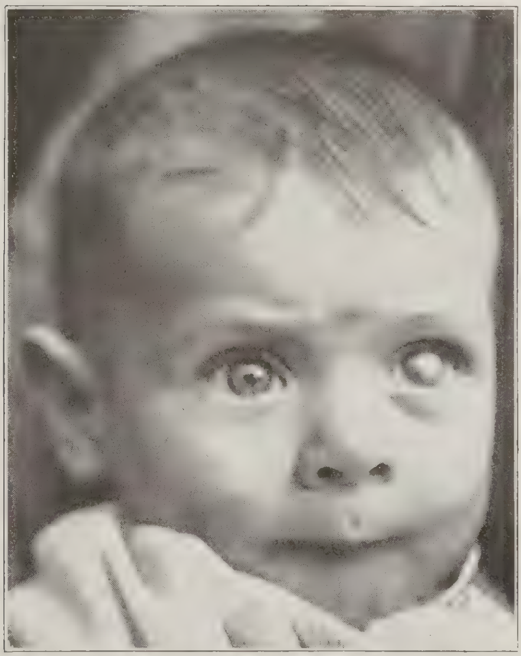

Fig. 4.—Recovery from xerophthalmia, showing permanent eye lesion.

If a small child receives no milk whatever, not even separated milk or buttermilk, but is given only water, tea, gruel and the like for a prolonged period, on account of diarrhea or some other malady, it will become wasted and atrophic, with dry wrinkled skin.

In this case, in addition to the absence of the fat-soluble A factor, several others were missing, but it is essentially the primary wasting disease, in this instance the intestinal trouble, which dominates the entire clinical picture. Such a case resembles most nearly the xerophthalmia described by the older authors.

When the child is a little older and stronger, and not ill, it can apparently thrive for a long time on infant food or other essentially carbohydrate diet, but sooner or later the tissues become edematous. and if the child has received no fresh milk, xerophthalmia, bronchopneumonia, etc., may supervene, just as in the first type.

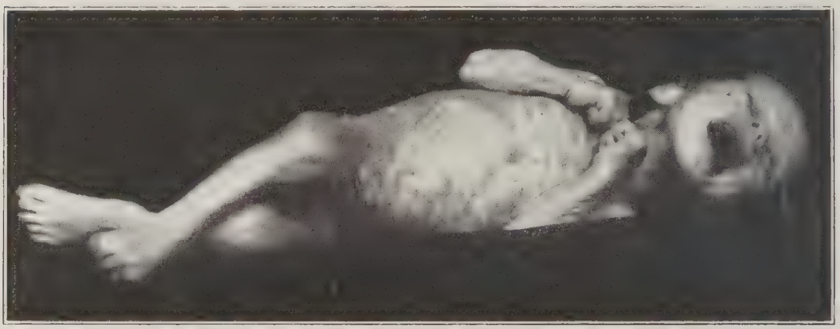

Fig. 5.—Atrophic child.

If the child has had only a little butter in addition to the carbohydrate diet, edema, such as that in chronic interstitial nephritis, can certainly occur, but neither xerophthalmia nor marked lessening of the powers of resistance is observed, and the child is easily restored to health when it receives milk. Figure 6 shows such a case, with an enormous amount of edema but with no eye lesion.

Besides the xerophthalmia, the characteristic symptoms in this disease, which arises in consequence of the absence of the fat-soluble A factor, are, therefore, inhibition of growth and diminished resistance and vitality. In older children and adults, who hardly utilize so much fat-soluble A factor as the small child, the disease may be attended merely by the latter symptoms. It is only when the lack of the fat-soluble A factor in the food has been almost absolute for a long time, or when the bodily requirement of it has been very great, e. g., in chronic infectious diseases, that older children develop xerophthalmia. It is chiefly young children, that is to say those under 2 or 3 years of age, that develop xerophthalmia, and this may happen even though there has been some fat-soluble A factor in their food.

During the war, there was much sickness among the older children in central Europe, which took the form especially of inhibition of growth, and a large number of infectious diseases running a grave course. Thus, many children were attacked by tuberculosis. The smaller children, on the other hand, were little affected, and xerophthalmia was scarcely ever seen in them. This state of affairs was due to the fact that during the war all the milk and milk products in Germany were rationed so that every little child obtained a certain amount daily. If the child was being suckled by the mother, she got the milk, and xerophthalmia was never observed in children suckled by a mother capable of yielding sufficient milk.

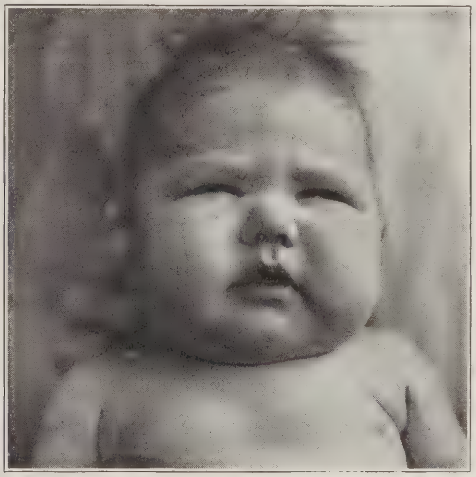

Fig. 6.—Edematous child.

In Denmark the conditions, as mentioned, were different. Before, and especially during, the war, there were many cases of xerophthalmia. In a recent investigation undertaken for the Danish Ophthalmologic Society by Olaf Blegvad, from 600 to 700 cases of xerophthalmia were found to have occurred between 1909 and 1920 among children, in a population of less than 3,000,000, and there were probably others.

The reason xerophthalmia was so widespread, despite the fact that Denmark did not take part in the war, is that this dairy-farming country manufactures and exports butter. During the war, butter, and consequently fresh milk, became so expensive that the poor could procure scarcely any of it, and they were able to obtain only separated and buttermilk, which could always be had at a low price. The number of cases of xerophthalmia increased, therefore, until 1918. In that year, the disease was suddenly checked, as will be seen from Figure 7. The reasons were several, but the principal cause was undoubtedly that in 1918, on account of the German blockade, butter was rationed in Denmark, so that every individual, including small children, was entitled to 0.25 kg. of butter a week, and as there was practically no pork fat or margarin in the country everybody had to eat butter. Xerophthalmia ceased simultaneously. These facts show as clearly as an experiment that the absence of the fat-soluble A factor is the cause of xerophthalmia.

After the termination of the war, the rationing of butter came to an end, and xerophthalmia returned, but its occurrence was rare as compared with its former incidence. It was particularly noticeable that the severe cases no longer occurred. The people and the Danish physicians had come to know the disease and had learned how to avoid and treat it.

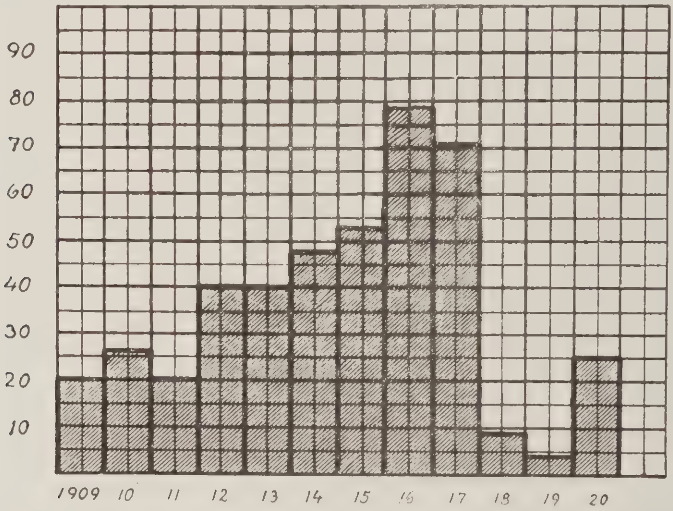

Fig. 7.—Frequency of xerophthalmia in Denmark (1909-1920).

The condition caused by lack of the fat-soluble A factor is cured by supplying the latter to the patients, best in the form of fresh milk, cream, butter or cod liver oil. The xerophthalmia is the first symptom to disappear. Then the child begins to thrive and infections are gradually overcome. The latter are therefore cured by the administration of the fat-soluble A factor. This is in harmony with the old clinical experience that chronic infectious diseases, particularly tuberculosis, are improved by a diet rich in fresh milk, butter and cod liver oil.

The fat-soluble A factor is thus particularly important not only for the eye lesion but also for establishing immunity, and it is clear that a great deal of it is required in infectious diseases.

Large quantities must also be consumed during the period of growth. This is most clearly evident from McCollum's animal experiments, but the study of xerophthalmia points in the same direction, as it occurs practically only in children; that is to say, in growing individuals. Moreover, the disease appears especially in the spring months, at which season the most marked growth of the child takes place, according to Danish investigations. The cases not occurring in this annual period of growth have always been complicated by serious infections or chronic diarrhea. This distribution of the cases is shown in Figure 8.

It has been thought that the increase in the number of cases in the spring was due to a different content of fat-soluble A factor in the winter milk (stall feeding) and the summer milk (grass feeding). It is possible that there is more of the fat-soluble A factor in the first "grass milk," and that this has something to do with the disappearance of the disease in the summer, but a decreased fat-soluble A content in the milk cannot be the cause of the many cases arising in the growth-period of the spring because precisely the same distribution of cases is found among patients that have received no milk or milk products at all for a long while. It is also difficult to believe that milk from healthy cows could be deficient in the fat-soluble A factor. At any rate, it has not yet been proved, and the experience of xerophthalmia in Denmark is against the supposition.

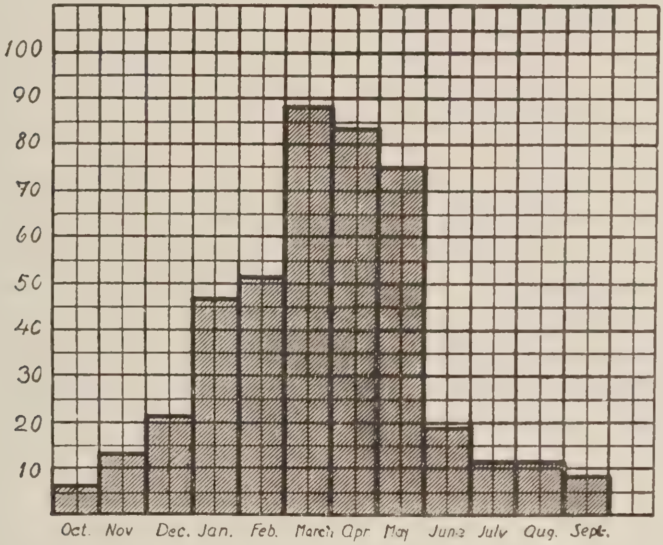

Fig. 8.—Seasonal variations of xerophthalmia in Denmark.

This special relation between the fat-soluble A factor and growth, and between it and infections, has not been thought to be confined to this body, but is also found in other deficiency diseases. Thus, Alfred F. Hess has especially pointed out that the relation is somewhat similar in the case of scurvy, the disease which arises from the absence of the antiscorbutic factor. Scurvy, like every other serious disease, is undoubtedly able to affect growth and diminish the power of resistance against infections; but in the disease caused by the lack of the fat-soluble A factor, both these features are very strongly emphasized, and in a special manner. Thus, scurvy, in contradistinction to xerophthalmia, is not particularly associated with childhood, nor does it, like xerophthalmia, occur especially during the annual growth period. Moreover, a statistical examination of my cases of scurvy shows that this disease is not associated with infections to nearly the same extent as is xerophthalmia.

CONCLUSIONS

Xerophthalmia and rickets are very rarely met with in the same child. Rickets can therefore hardly be due to the absence of the fat-soluble A factor.

What I have said here and have proved to you testifies to the enormous importance of milk as a food for the child. No other article of diet can replace milk. Absence of milk from the diet or the inclusion of improperly modified milk is the origin of most serious diseases.

By employing milk, and especially cream and butter, in the diet, not only is this terrible eye disease, which I believe will be discovered in every country when it is looked for, cured, but growth and development are promoted, and the cure of our most prevalent infectious diseases is advanced.

A CLINICAL STUDY OF RICKETS IN THE BREAST-FED INFANT *

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In the practice of pediatrics, one frequently finds rickets in the breast-fed infant. On close questioning, there may or may not be elicited some error in the feeding. If there is an error, it is likely to be blamed for the disease; and if there is no error, the history is very likely to be regarded as doubtful as regards some points. This study was undertaken to ascertain the incidence of rickets in breast-fed babies, and to investigate the symptoms and the influence of the disease in those whose feeding and care was supervised and directed from birth.

In my service of the newly born, with its followup clinic, at the Touro Infirmary, an opportunity is afforded to study those infants whose care is begun at birth and closely supervised and regulated thereafter. This service has been described elsewhere.[1] Suffice it to say that it includes an inside and an outside division and a followup outpatient department. The inside division includes (*a*) the care of all the infants born in the obstetric service, (i. e., the free patients), with the responsibility for the baby's welfare beginning at the time the cord is cut; and (*b*) the complete supervision of the breasts of the mother. The outside division in like manner includes those babies born in the home and delivered by the outside obstetric service of the institution. These babies report to the outpatient followup clinic on the Thursday nearest which they are 4 weeks old, and return every fourth Thursday thereafter. There is a social service operating in connection with the department so that a close association with the families is had.

Those eligible to this free service include families whose earnings do not exceed $100 a month.

The inside division includes only white patients, there being no provision for colored patients; the outside division, both the white and colored. The service, then, includes members of both races whose earning capacity it is believed warrants free care.

This service of the newly born, which was begun nearly two years ago, is increasing rapidly in size. This study extended over the period of the first year of its operation. Recently, our maximum attendance was reached when, on one Thursday morning, ninety-one babies were seen.

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* Received for publication, Nov. 2, 1923.

* From the service of the newly born, Touro Infirmary, and the Department of Pediatrics of the School of Medicine of Tulane University of Louisiana.

[1] DeBuys, L. R.: South. M. J. **15**:115-120 (Feb.) 1922.

In the observations included in this study, routine examinations were made of each and every baby for clinical evidences of rickets. These observations were made by another observer and checked by me, the readings being practically always the same.

Rickets is an extremely interesting disease and one of which it may be said that the more it is studied, the more obscure its etiology appears to be. It has its pathologic, serologic, roentgenologic and clinical findings. Routine observations in this study included rickets only in its clinical manifestations. The clinical evidences of rickets included were bosses, craniotabes, costal beading, lateral flattening of thorax, flaring ribs, epiphysial enlargements and bow-legs. Observations were also made on the growth and development of the children investigated, including measurements of height, weight, head, chest and abdomen, and their period of dentition. The ages at which they sat alone, stood alone and walked alone were also noted, as well as their condition of general nutrition.

This study included observations covering a period of one year, made on 197 babies, sixty-two white and 135 colored. Twelve calendar months were selected as the period, in order to include the seasonal influences.

It had been found that greater cooperation and better results were obtained with the method of feeding employed as a routine in the pediatric service of the institution; hence, it was chosen as a uniform one in this investigation. It consisted in a two hour interval feeding for those babies whose weights were under 9 pounds (4,082.3 gm.); a two and one-half hour interval for those whose weights were between 9 and 12 pounds (5,443 gm.), and three hour interval for those weighing 12 pounds and upward, only one breast being fed at a time and no feeding exceeding twenty minutes. This did not mean that each baby had to be kept at the breast for the twenty minutes, but only so long as he showed an inclination to nurse vigorously. Occasionally a baby is encountered who has to be encouraged to nurse, and in these instances, the length of the feeding was not to exceed twenty minutes. We have shown to our satisfaction that, in the twenty-minute nursings, the bulk of the food is usually obtained within the first ten minutes, and that in the second ten minutes very little food was taken. The last milk obtained, however, consists of strippings, which are rich in fats, and this element being necessary, the twenty-minute feedings were advocated. When the breast milk was thought to be insufficient because of no gain in the baby's weight, and there was no disease in the patient, observations were made on the breasts by weighing before and after nursing. When necessary, complemental feedings were added. Seventy-four per cent. of the white mothers were able to nurse their babies exclusively for three months; 37 per cent. were able to nurse their babies exclusively for six months. Seventy-eight per cent. of the colored mothers were able to nurse their babies exclusively for three months; and 20 per cent. were able to nurse their babies exclusively for six months.

As a rule, cereal jellies and toast were begun when the baby was 6 months old, or when its weight was 15 pounds (6,803.9 gm.). Orange juice was invariably begun as soon as any food other than breast milk was added to the baby's diet. Broths were begun at about 9 months, and strained vegetables toward the end of the year.

In no case was cod liver oil given before marked evidence of rickets was noted. In only thirty-nine instances was it begun within the first three months, twelve of which were in white and twenty-seven in colored children; in seventy-five instances, before the sixth month, twenty-six of the babies being white and forty-nine colored, and in 107 instances in the series, cod liver oil was begun before the twelfth month, thirty-nine of the babies being white and sixty-eight colored.

The diet of the mother was not restricted. Fruits and vegetables in season, as well as beans and peas and meats, constituted the major part of the dietary, this being, of course, influenced by the income.

Hygienic measures other than those having to do with the feeding, and including airing, bathing, exercise, clothing, rest and habits were advised, and in many instances, the cases were referred to the social service for investigation and supervision.

It was noted that those babies who remained away from the outpatient followup clinic returned invariably with evidence of more advanced rickets than was found in those cases constantly under supervision for a like period. It was also noted that in these cases there was a direct relation between the severity of the rickets and the interval of nonsupervision. In only two instances were the babies referred to the general clinic because of not following directions. Both children were colored. Only forty-two of the babies suffered some minor acute illness during the entire year. Thirteen of these were white and twenty-nine colored. There was no relation between these acute ailments and any increase in the symptoms of rickets.

Of the white babies studied, 47 per cent. were first born, 16 per cent. were second born and the remaining number ranged from the third to the twelfth born. Of the colored infants, 46 per cent. were first born, 21 per cent. were second born, and the remaining number included those up to the tenth born.

All infants showing any suggestive manifestations of syphilis were examined serologically, and in eight instances postive Wassermann reactions were obtained, two in white and six in colored children. There was no apparent relation between these cases and those presenting either the least marked or most marked evidence of rickets.

Sex played no part in the incidence, or in the severity of the symptoms.

The climate of New Orleans is rather mild, there being only a very short period during which one is deprived of the benefits of being out doors. During the investigations, the winter was especially mild. Taking the attendance at the clinic as the index to the weather, the instinct of the mother determining whether the baby should be out or not, there was no definite curve, clearly showing that seasonal influence need not be considered.

From a study of the atmospheric conditions during the period of this investigation (Table 1), it will be noted from the percentage of possible sunshine that there was 3.9 per cent. more sunshine than the normal average for the same period. The average temperature was 1.7 degrees (F.) higher for the year. The average atmospheric pressure reduced to sea level was 0.6 inch less than the average mean for the year. The total precipitation for the period of study was 4.23 inches less than the normal average, and the humidity was normal average. These facts are interesting as the amount of rickets in this study occurred with increased sunshine, increased temperature and diminished precipitation as compared with the normal average.

TABLE 1.—*Monthly Meteorologic Summary*

	Possible Sunshine		Percentage of Temperature (F.)		Atmospheric Pressure			Precipitation (Inches)		Humidity			
						Since 1871				In Study			
	Average in Study	Average 1891-1916	Average in Study	Normal Average	Mean in Study	Highest	Lowest	Total per mo. in Study	Normal	7 a.m.	7 p.m.	Normal 7 a.m.	Average 7 p.m.
October....	88	64	71.2	69.5	30.0	30.55	28.11	1.82	4.81	73	62	80	72
November..	64	55	66.6	60.6	30.1	30.68	29.47	3.83	3.79	85	72	82	74
December..	57	45	60.8	54.4	30.13	30.71	29.55	3.49	4.46	86	74	82	75
January...	36	48	51.0	53.0	30.14	30.80	29.27	5.22	4.63	86	81	82	74
February..	49	49	62.8	56.3	30.12	30.71	29.13	3.25	4.47	86	78	82	73
March......	62	57	62.5	62.0	30.08	30.71	29.55	8.45	5.30	86	76	82	73
April.......	61	59	73.3	67.9	30.05	30.48	29.44	3.81	4.90	81	68	82	71
May........	54	64	75.7	74.5	29.93	30.38	29.62	5.75	3.88	84	77	81	71
June.......	57	61	81.8	79.6	29.99	30.34	29.62	6.45	6.16	81	72	81	75
July........	63	53	82.4	81.3	30.06	30.29	29.41	4.05	6.47	84	75	82	76
August.....	70	55	83.0	82.2	29.97	30.29	29.43	5.71	5.61	84	72	82	77
September.	70	61	80.8	79.2	30.00	30.31	28.11	0.93	4.81	83	71	82	75
Average for year....	60.9	57	70.9	69.2	30.05	30.52	28.39	52.79	57.02	83	73	82	74

Of the 197 babies studied in all, there was at least one plus finding in the symptoms of rickets. These plus findings ranged from one in any one of the symptoms to a total of nine and one half in the combined symptoms in the white and ten in the combined symptoms in the colored. There were only three instances in this study in which there were one plus readings, two in the white and one in the colored. In each instance, the symptom thus noted was beading.

None of the individual clinical symptoms appeared to have a seasonal peak, but considered from the total peaks as reckoned from the greatest number of plus readings of all the clinical symptoms, there was a seasonal incidence of maximum findings as follows: The four weeks' period of maximum findings was from March 9 to March 29; six weeks' period, March 9 to April 13; eight weeks' period, February 9 to March 29; ten weeks' period, February 9 to April 13; twelve weeks' period, January 26 to April 13; fourteen weeks' period, January 12 to April 13; sixteen weeks' period, January 5 to April 20; eighteen weeks' period, December 29 to April 27; twenty weeks' period, December 29 to May 11; twenty-two weeks' period, December 29 to May 25; twenty-six weeks' period, December 8 to June 1. It will be seen that March was the month during which the seasonal manifestations of the disease was most marked. The disease was more marked during the half year from December 8 to June 1, the March peak being a little beyond the middle of the period.

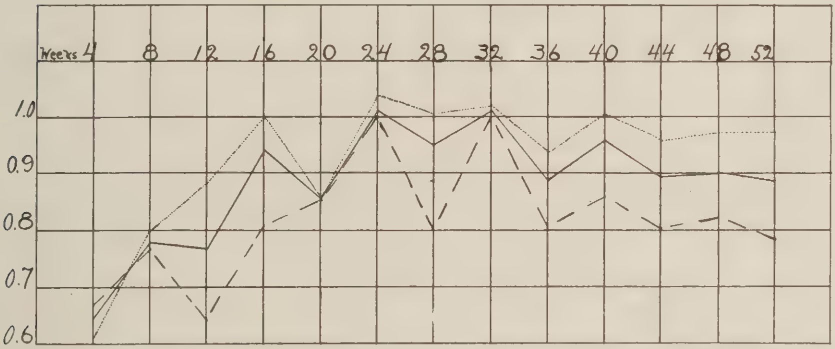

Chart 1.—Average intensity of symptom of beading throughout the first year. In this chart and the charts following, the broken line is the curve for white infants; the dotted line that for the colored infants; the solid line represents the average for the two races. The figures at the top represent the number of weeks and the figures at the left (Charts 1-6) the amount of plus reading.

The symptoms in the order of their frequency were beading, epiphysial enlargement, cranial bosses, flaring ribs, craniotabes, lateral flattening of the thorax and bow-legs. Lateral flattening was usually associated with the flaring ribs and was not especially studied separately. It was markedly evident in many instances. Bow-legs were noted in several instances but as this symptom could not be proved by exact methods, as for example, the roentgen ray, it was not gone into especially.

Beading was by far the most frequently met symptom, occurring in 97 per cent. of the white and in 98.9 per cent. of the colored. Chart 1 shows its severity according to age by weeks, both in the white and in

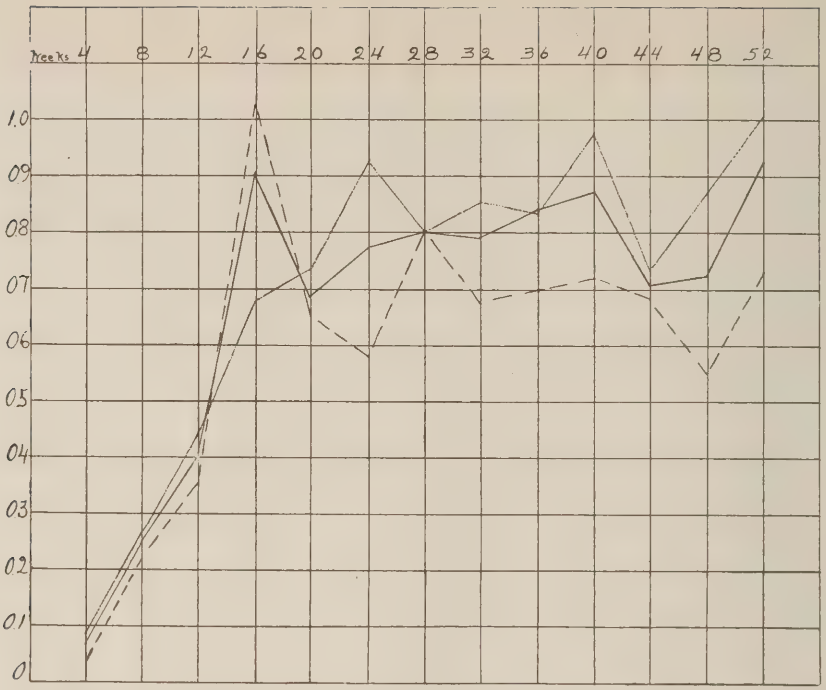

Chart 2.—Average intensity of symptom of enlarged epiphyses throughout the first year.

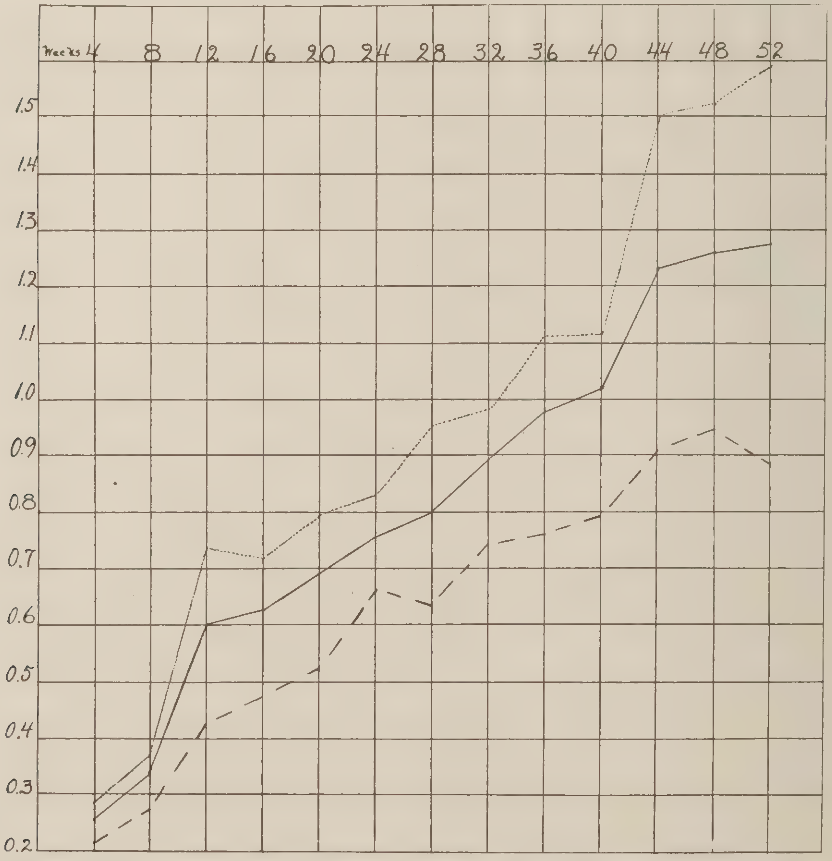

Chart 3.—Average intensity of symptom of cranial bosses throughout the first year.

the colored, and the average for the study. In the white, it was first noted as early as the fourth week, and it was also first noted as late as the thirty-second week. In the colored, it was also first noted as early as the fourth week, but it was first noted as late as the thirty-sixth week.

The beading curve shows a steady increase in incidence up to the end of the year.

Epiphysial enlargement is the symptom next in frequency, occurring in 84 per cent. of the white and in 87.1 per cent. of the colored. It was first noted as late as the thirty-sixth week, and as early as the fourth week in the white; and in the colored, it was first noted as late as the thirty-sixth week and as early as the fourth week. Chart 2 shows its severity according to age by weeks.

Cranial bosses showed an incidence of 68.63 per cent. in the white and 75.27 per cent. in the colored. It was first noted in both the white and colored at 4 weeks, and the latest age at which it was first noted in the white was 40 weeks and in the colored 32 weeks. This curve in Chart 3 shows a steady increase in the severity of the condition, with a rapid ascent toward the end of the year.

Flaring ribs showed an incidence of 62.58 per cent. in the white and 78.04 per cent. in the colored. In this symptom, the difference in its occurrence in the two races was greater than that of any of the symptoms, it being nearly 15 per cent. more frequent in the colored. It was first noted in both the white and the colored as early as the fourth week. The latest age at which it was first noted was 32 weeks in the white and 36 weeks in the colored. The curve in Chart 4 shows decidedly greater severity of this symptom in the colored over the white throughout the year.

Craniotabes, as shown in Chart 5, is extremely interesting. Its incidence of 33.33 per cent. in the white and of 43.48 per cent. in the colored is the least frequent of the principal symptoms. The curve of the severity of the symptoms, with its rapid ascent, short period of existence and its abrupt decline, is striking. It was first noted in both the white and colored at the age of 4 weeks, and was first noted as late as the sixteenth week in the white and twenty-fourth week in the colored.

It will be seen from the foregoing that each of the symptoms was first noted as early as the fourth week, and with the exception of craniotabes, was first noted as late as from the thirty-second to the fortieth week. The cranial bosses were the latest symptom to be first noted.

The relative occurrence of the symptoms in the races is also interesting. In the beading, the difference is only 1.9 per cent. This is the most common symptom in both races, and its incidence is most nearly the same. The difference in the frequency of the individual symptoms in the white and colored increases as the frequency of the symptoms decreases, with the exception of craniotabes.

It is worthy of note that each symptom has a greater incidence in the colored, and in Chart 6, in which the severity of the combined symptoms is recorded, the curve is more even, with fewer variations in the curves of both the white and the colored, the curve of the colored being constantly above and that of the white always below the average for this study.

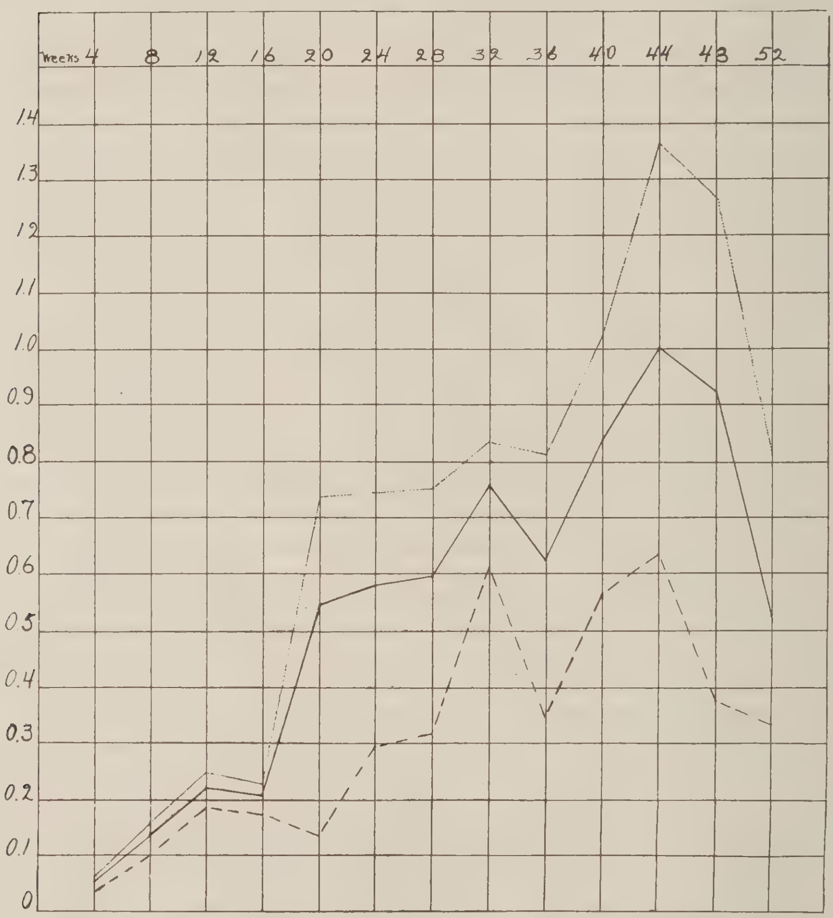

Chart 4.—Average intensity of symptom of flaring ribs throughout the first year.

It is of especial interest to note how early (during the first three months) and rapidly rickets develops. It must not be looked on as a

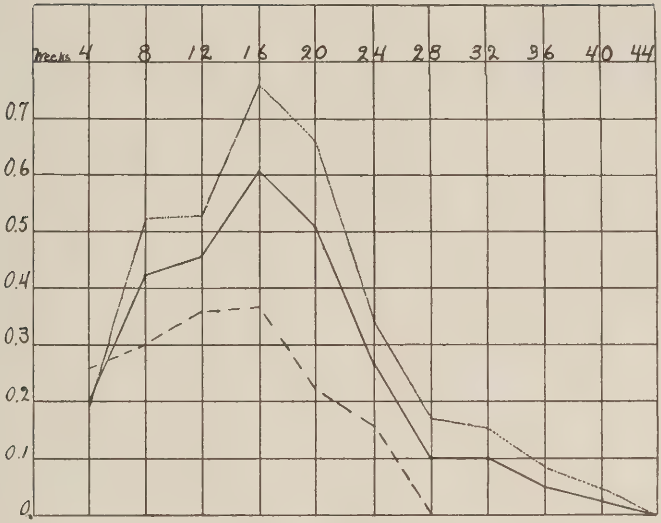

Chart 5.—Average intensity of symptom of craniotabes throughout the first year.

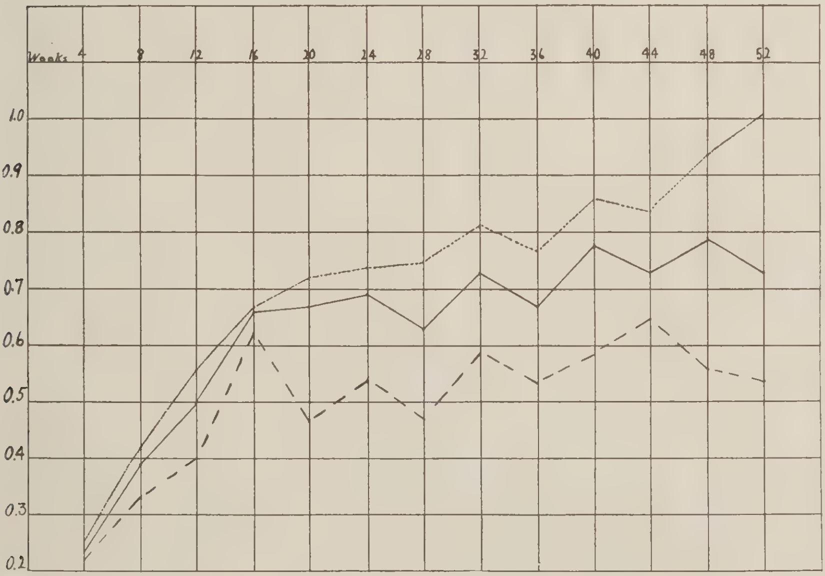

Chart 6.—Average intensity of combined clinical symptoms of rickets throughout the first year.

disease of the second half of the first year, but a disease which may begin shortly after birth.

The influence of rickets, as it occurs in the breast-fed, on the growth and development was also studied.

The average height of the white children was that of the normal average. The colored children were shorter than the white throughout the year. The height measurements in this study showed the most even curve of all the measurements. The most marked cases of rickets and the mildest cases were studied. Between the heights of these children and the general average, there were no noticeable differences.

The weight curve of the white children was a little above the normal average. In the colored, it was not satisfactory, its variations for the different ages being rather confusing, more particularly toward the latter part of the year. These variations may have been due to a lack of uniformity in feeding methods. The weights of the children suffering from marked rickets were below the normal average, while the weights of those with the mildest cases were about normal.

Table 2.—*Tissue Turgor (Percentage)*

	Excellent	Good	Fair	Poor
White	4	59.1	26.5	10
Colored	...	68.4	27.1	4
Average	1.4	65	27	6

The head measurements in the general average of the white in the study were a little greater at birth, but soon approximated the normal average and continued so thereafter. In the colored, the general average in early measurements was slightly greater but the increase throughout the year was below normal, so that at the end of the year the head was smaller than the normal average. The head measurements in the most severe and mildest cases of rickets in the white infants did not vary to any degree from the general average. In the cases of severe rickets in the colored, however, in the early months, there was a decided increase, and at the end of the year the measurement of the head was a half inch greater than the normal average.

The chests of the white infants in the general average were approximately normal. In the colored, at the end of the year, the chest measurement was less than normal. The differences in degree of severity of the rickets apparently did not cause any great variations in the chest measurements.

The measurements of the abdomen in the general average in the study in both white and colored infants were smaller than those of the chest. In the cases of marked rickets, the abdomens were larger than the general averages, and in the mildest cases they were about the same for both white and colored.

Tissue turgor as an indication of the state of nutrition of the infants was noted in Table 2. It was found that in only 4 per cent. was it excellent, and these cases were all in white children. There were, however, more colored with good or fair tissue turgor than white, 68.4 and 27.1 per cent., respectively, as compared with 59.1 and 26.5 per cent. in the white. The grade of tissue turgor did not seem to be influenced by the severity of the rickets.

Dentition as shown in Chart 7 began a little earlier in the colored than in the white, the first tooth erupting at the twentieth week in the former and at the twenty-fourth week in the latter. The age of latest eruption of the first tooth in this study was 44 weeks in the white and 48 weeks in the colored, the average age of eruption of the first tooth being 32 weeks in the white and 33⅓ weeks in the colored. It will be seen from Chart 7 that the colored infants began to teethe earlier, and the teething curve rises steadily up to the forty-fourth week, when it passed that of the white infants. Teething in the white infants began four weeks later, assumed the lead at the twenty-fourth week and retained it up to the forty-fourth week. At the end of the year, the colored infants averaged one tooth more than the white.

In this study, the severity of the rickets did not seem to have any special influence on dentition, as shown in the comparison of the dentition in the most marked with the least marked cases of rickets, except that in the colored infants those with mildest rickets had more teeth, and at an earlier date. The influence of the severity of rickets on dentition is noted in the following tabulation:

DENTITION IN MARKED RICKETS

In the white, earliest eruption of first tooth, 28 weeks.
In the white, latest eruption of first tooth, 48 weeks.
In the white, average time eruption of first tooth, 38½ weeks.
In the colored, earliest eruption of first tooth, 28 weeks.
In the colored, latest eruption of first tooth, 52 weeks.
In the colored, average time of eruption of first tooth, 38½ weeks.

DENTITION IN LEAST RICKETS

In the white, earliest eruption of first tooth, 28 weeks.
In the white, latest eruption of first tooth, 52 weeks.
In the white, average time eruption of first tooth, 38½ weeks.
In the colored, earliest eruption of first tooth, 24 weeks.
In the colored, latest eruption of first tooth, 40 weeks.
In the colored, average time of eruption of first tooth, 29½ weeks.

There were no instances of abnormal teeth in this series.

Observations on the muscular development as shown by sitting alone, standing alone and walking alone did not reveal anything unusual.

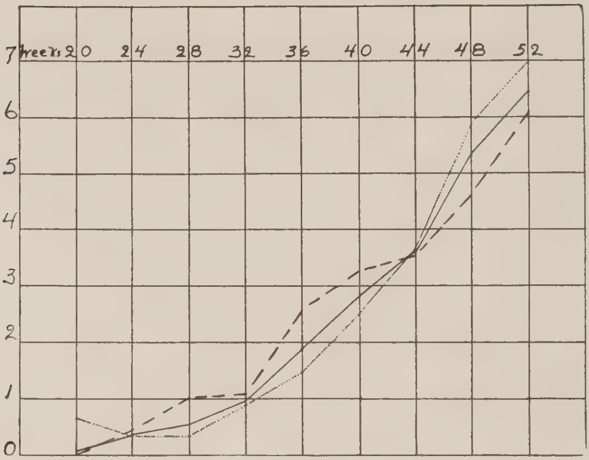

Chart 7.—Average number of teeth (figures to left of chart).

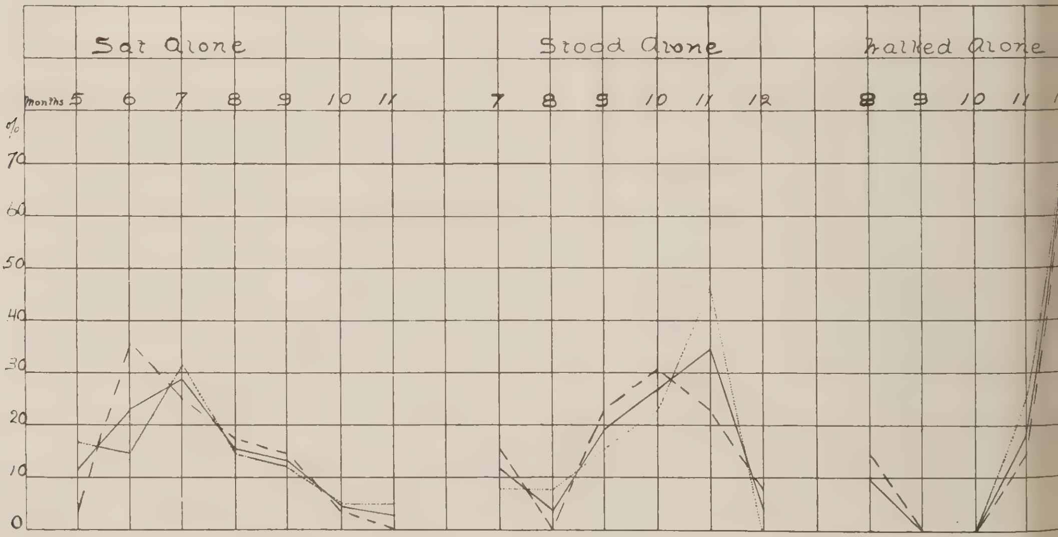

Chart 8.—Muscular development. The figures to the left represent the percentage of children.

In Chart 8, it will be noted that 35 per cent. of the white babies sat at 6 months, while only 31 per cent. of the colored could sit alone at 7 months. However, 17 per cent. of the colored babies sat alone at 5 months, while only 3½ per cent. of the white could do so. The greater number of white stood alone earlier than the colored—30.7 per cent. of the white stood alone at the tenth month, while 46 per cent. of the colored could stand alone at 11 months. Fifteen per cent. of the white were able to stand alone at 7 months, as compared with 7.6 per cent. of the colored.

The white infants began earlier to walk about, but the colored at the tenth month passed ahead of the white and remained in the lead thereafter.

SUMMARY

1. Only those cases in which the symptoms of rickets were noted before complemental feedings were instituted were included in this study.
2. Cod liver oil was not given in any case before there was unmistakable evidence of the existence of rickets.
3. Lack of supervision and care seemed to cause the rickets to develop with more intensity. There was a direct relation between the severity of the rickets and the interval of nonsupervision.
4. There was no noticeable increase in the symptoms of rickets after simple acute illnesses.
5. There was no apparent relation between the severity of the rickets and the numerical order of the child in a family, or the number of the children in a family.
6. Syphilis was noted in only eight instances as determined by the clinical manifestations of the disease and the Wassermann reaction. There was apparently no relation between syphilis and the severity of the rickets.
7. The atmospheric conditions during the period of this study showed that the amount of sunshine was greater and the temperature higher than the normal average; that the precipitation and atmospheric pressure were less than the normal average, and that the humidity was the normal average.
8. According to the clinical manifestations of rickets, the disease was present in every case in this study.
9. The disease was more marked in the colored subjects than in the white.
10. There was no seasonal peak for any of the individual symptoms. There was, however, a seasonal peak of the combined symptoms of the disease noted in the month of March.
11. Costal beading was the most frequent symptom. Enlarged epiphyses, cranial bosses, flaring ribs and craniotabes followed in the

order named. The short period of the existence of craniotabes, with its rapid increase and abrupt decline, was striking.

12. Each symptom was more common in the colored than in the white. Beading showed the least difference, i. e., 1.9 per cent. The differences increased as the frequency of the individual symptom decreased with the exception of craniotabes.

13. Rickets should not be looked on as a disease of the second half of the first year, but as a disease which may begin at least shortly after birth.

14. In the study of the influence of rickets on the growth and development of the child the following were the outstanding notations:

(*a*) The heights of the white babies were normal average, the heights of the colored were less.

(*b*) The weights of the white babies were a little above the normal average. The weights of the colored varied so much for the different ages that they were unsatisfactory for comparison. The weights of the markedly rachitic were below the normal average.

(*c*) While there were some slight variations in the measurements of the head, the most significant was the increased size of the markedly rachitic colored.

(*d*) The chests of the colored were smaller than the normal average.

(*e*) The abdomens in this study were smaller than the normal average. In the markedly rachitic, the abdomens were larger than the general average.

(*f*) Tissue turgor was recorded as excellent only in the white. It was noted as poor more frequently in the white than in the colored.

(*g*) Dentition began earlier in the colored, and at the end of the year the average number for the colored was greater than for the white. Aside from the fact that the colored with the mildest rickets had more teeth and had them earlier, nothing was noted in the study as to the influence of the severity of the rickets on dentition.

(*h*) A study of the muscular development as recokoned by the ability to sit alone, stand alone and walk alone showed some slight variations between the white and colored. It showed nothing of significance between the least marked and most marked cases of rickets.

REVIEW OF THE LITERATURE FOR 1921 AND 1922 ON NEUROLOGY OF CHILDREN *

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ACUTE POLIOMYELITIS

Recent studies of Wahler [238] confirm the experience of others that the prognosis for the acute stage of poliomyelitis is favorable in the absence of symptoms of a lesion of the medulla oblongata. Very marked and extended paralyses at this stage as a rule become regressive and limited to definitely circumscribed foci. The prognosis for the post-acute stage as to restitution is doubtful. Those cases that were discharged with no or with insignificant improvement revealed practically no farther amelioration even with orthopedic and surgical treatment during the observation of from two to three years. In the cases showing a marked tendency toward improvement at the end of the acute stage, late reexamination revealed an additional, often striking, improvement, perhaps due to continued treatment. The prevention of deformities is of great importance, and children must be kept under observation during the entire growing period.

Paralysis affecting the upper extremities is milder and more amenable to improvement than that affecting the lower extremities. The improvement is most rapid in the first year, but under treatment may continue for four years, as the analysis of 180 cases by Lovett [239] demonstrates. In lower extremities, after the third year, there is a tendency to a slight loss of muscular power, partly due to deformities, an effort to prevent which must be made by every possible means.

Children with extensive paralysis following poliomyelitis develop certain types of locomotion. Magnus' [240] patient had acquired the locomotion of a quadruped with such agility that he presented a picture "not unlike that of a chimpanzee." In a very rare group, the afflicted become "hand-walkers." A unique case of this type, in an 11 year old boy, is reported by Kopits.[241] The lower extremities had been paralyzed since his second year. As two striking illustrations to the text demonstrate, the boy used the upper extremities as active support, for locomotion exclusively, maintaining his equilibrium either by "assuming an

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* Received for publication, Oct. 6, 1923.

[238] Wahler, F.: Arch. f. Kinderh. **69**:343 (May) 1921.

[239] Lovett, R. W.: Third Year in Infantile Paralysis, J. A. M. A. **77**:1941 (Dec. 17) 1921.

[240] Magnus, G.: Arch. f. Orthop. **19**:50, 1921.

[241] Kopits, E.: Jahrb. f. Kinderh. **99**:268 (Sept.) 1922.

attitude resembling that of a standing bird" or by lifting his trunk into almost erect posture with the pelvis high up, from which the paralyzed legs dangle down. He displays a remarkable dexterity in playing ball, running and fighting, for instance.

Berghinz [242] encountered a girl who employed mirror writing or wrote normally at will with the left hand, following right hemiplegia from poliomyelitis; and Babonneix and Pollet [243] describe crossed localization of the paralysis involving the right arm and left leg, with marked changes in the bones and extreme hypotonia of the muscles.

The occurrence of four cases of poliomyelitis in the same family is reported by Mulsow and Matousek.[244] The source remained unknown.

As paralysis or weakness of the gluteal muscles, of the hip flexors and abdominal muscles, is of primary importance as a cause of lameness, operations on the thigh or the leg should be undertaken only, as Lovett [245] emphasizes, after careful study of the gait and with the understanding that the hip and abdominal lameness will not be affected materially by the procedure. The same author,[246] basing his conclusions as to diagnosis, prognosis and treatment on a study of 5,100 cases, emphasizes that early treatment consists of rest; that in the convalescent phase muscle fatigue is our chief danger and muscle reeducation our chief reliance, and that deformities prevent proper function and promote muscular deterioration.

The therapeutic procedure recommended by the Harvard Infantile Paralysis Commission, which consists chiefly in maintaining from the start the greatest rest and fixation obtained by recumbency, frames and splints, has been criticized by Feiss.[247] On physiologic principles, in order to prevent muscular deterioration by disuse, he urges early application of function by willed effort and reflex movements, the latter especially in infants.

The report of the Harvard Infantile Paralysis Commission published by Peabody,[248] reviewing the therapeutic results since 1916, fails to convince the Commission of the value of treatment in the preparalytic stage with intravenous injections of serum from patients who have recovered from this disease.

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[242] Berghinz, G.: Pediatria **29**:301, 1922.

[243] Babonneix and Pollet: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:778 (May 27) 1921.

[244] Muslow, F. W., and Matousek, W. J.: Family Outbreaks of Poliomyelitis, J. A. M. A. **76**:159 (Jan. 15) 1921.

[245] Lovett, R. W.: Surg., Gynec. & Obst. **32**:20 (Jan.) 1921.

[246] Lovett, R. W.: Diagnosis, Prognosis and Early Treatment of Poliomyelitis, J. A. M. A. **78**:1607 (May 27) 1922.

[247] Feiss, H. O.: Treatment of Early Infantile Paralysis as Based on Physiologic Indications, J. A. M. A. **78**:85 (Jan. 14) 1922.

[248] Peabody, F. W.: Boston M. & S. J. **185**:174 (Aug. 11) 1921.

According to Henderson[249] of Rochester, surgery is indicated only in residual paralysis, and only 25 per cent. of such patients can be helped by surgical procedures. The author discusses the various methods of dealing with the conditions by manipulations, tenotomies, arthrodeses, etc.

That nurses and physicians may transmit the virus, either by being affected themselves or by being healthy carriers, should be kept in mind. The experiences of Wallgren,[250] who himself has been a carrier, and the experiences of others cited by him warn anew of this possibility. As the disease is transmitted greatly by healthy carriers, home disinfection is no preventive measure, as pointed out by Mueller[251] in an article on the epidemiologic factors in the disease. Saunders[252] incriminates the fly *Lucilia Cesar* as playing a rôle in the propagation of the disease, maintaining that, in the absence of this insect, poliomyelitis is no more to be feared than malaria fever without anopheles.

ENDOGENOUS (HEREDITARY FAMILIAL) DISEASES OF THE NERVOUS SYSTEM AND THE MUSCLES

Familial Amaurotic Idiocy.—The studies of this disease by Marinesco[253] apparently sustain the assumption that the histopathologic changes in the brain are the expression of a disturbance of the activity of intracellular ferments, the swelling of the cells depending on hydrolysis produced by exaggerated activity of a protease.

The symptomatology and pathology of three atypical cases of Tay-Sachs' disease are minutely described by Torrence.[254]

Paterson[255] reports the occurrence of familial cerebral degeneration affecting eight children of a gentile family, beginning at the age of from 3 to 4 months and ending fatally. In the one case described, the diagnosis of familial amaurotic idiocy was made.

Friedreich's Ataxia.—This disease in two of five children in a full blooded negro family, a very rare occurrence in this race, was observed by Lloyd and Newcomer,[256] and Hess[257] saw the disease in twins.

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[249] Henderson, M. S.: Surgery in Infantile Paralysis, J. A. M. A. **79**:1714 (Nov. 11) 1922.

[250] Wallgren, A.: Upsala Läkaref. Förh. **27**:45, 1922; abstr., Zentralbl. f. Kinderh. **14**:539, 1923.

[251] Mueller: Deutsch. med. Wchnschr. **48**:1569, 1922.

[252] Saunders, E. W.: Missouri M. A. J. **18**:160 (May) 1921.

[253] Marinesco, G.: Encéphale **16**:561 (Dec.) 1921; abstr., J. A. M. A. **78**:688 (March 4) 1922.

[254] Torrence, H. W.: Glasgow M. J. **15**:341 (June) 1922; abstr., J. A. M. A. **79**:504 (Aug. 5) 1922.

[255] Paterson, D.: Proc. Roy. Soc. Med. **15**:46, 1922.

[256] Lloyd, J. H., and Newcomer, H. S.: Friedreich's Ataxia, Arch. Neurol. & Psychiat. **6**:157 (Aug.) 1921.

[257] Hess, J. H.: M. Clinics N. America **5**:1749 (May) 1922.

Ataxia symptoms of the tabetic-spastic-cerebellar type, as described by Oppenheim, Concetti, Taylor, Gordon and others, were recorded by Orrico[258] in two boys of five, since they began walking. Discussing the similarity to and difference from the syndromes of Friedreich and P. Marie, the author insists that these clinical pictures should be distinguished from both types. The affection involves the posterior cerebellar tracts and the pyramides.

Bergmann[259] reports three Swedish agricultural families with Friedreich's ataxia and one with Marie's type. In one of the families, six children of fifteen, and in another four of eleven, presented the anomaly.

That not only a familial factor but also other pathogenetic elements, such as cerebrospinal processes due to syphilis or inflammations of other infections, can play a rôle in the causation of Friedreich's syndrome is again substantiated by the observation by Urechia and S. Mihalescu[260] of this symptom complex in a boy, due to acquired syphilis; and Linder[261] cites congenital syphilis under the picture of hereditary ataxia, presenting a rare combination of Friedreich's and Marie's type in a girl 6½ years old. This case, as that of Allen Star, is unique in the medical literature.

The relationship of congenital Friedreich's disease to other heredodegenerative affections is obvious in the association of the syndrome with nuclear paralysis of ocular muscles and with chorioditis disseminata observed by Schob.[262] Typical cerebellar symptoms were combined with an affection of the posterior spinal tracts and kyphosis. Remarkable was the presence of the same eye disturbances in the sister, the lack of progression and the absence of any hereditary or familial character except for the eye disturbances.

In one of the cases of Sanchis Banús and S. Gonzáles Taez (Arch. neurobiol. **3**: 43, 1922, Friedreich's symptom complex was combined with progressive cerebellar dissynergia; in the other, the latter condition existed in its pure form.

Progressive Myopathia.—Four brothers under 13 years of age affected with primary progressive myopathia and presenting different stages of the disease are the subject of a report by Auricchio.[263]

Duken and Weingartner[264] describe progressive spinal atrophy of Werdnig-Hoffmann type, in a boy 4½ months old, beginning probably in intrauterine life. A rare symptom in this affection, paradoxic thoracic respiration due to paralysis of the musculature of the thorax, was of special interest. Postmortem examination revealed, in addition to degeneration of the ganglion cells of the facial nerve and other nuclei, of the anterior horns, and of Clarke's columns, cavities in the entire spinal cord formed by dilated capillary lymph spaces or empty ganglion cell beds, and heteropias of white substance and ganglion cells. The author sees the basis of the affection in a constitutionally substandard abiotrophic central nervous system with extremely lowered resistance for functional tasks.

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[258] Orrico, J.: Arch. latino-am. de pediat. **16**:799, 1922.

[259] Bergmann, E.: Upsala Läkaref. För. **26**:1, 1921.

[260] Urechia, C. L., and Mihalescu, S.: Ztschr. f. ges. Neurol. u. Psychiat. **71**:207, 1921.

[261] Linder, C.: Jahrb. f. Kinderh. **100**:65, 1922.

[262] Schob, F.: Ztschr. f. ges. Neurol. u. Psychiat. **73**:188, 1921.

[263] Auricchio, L.: Pediatria **30**:488 (June 1) 1922.

[264] Duken, J., and Weingartner, A.: Ztschr. f. Kinderh. **29**:245, 1921.

Thomsen's Disease.—This disease existing in three generations is analyzed in great detail by Rosett.[265]

Periodic Myoplegia.—Neustädter [266] gives the interesting history of a family with several members suffering from periodic paralysis or insanity, and reports a case in full detail. This patient, 18½ years old, had since the age of 14 periodic paroxysms of marked weakness involving all the extremities, the trunk and neck, lasting from night till afternoon and being associated with fatigue, vomiting, headache and perspiration.

PERIPHERAL NERVES

Among forty-five cases of obstetrical palsies of the brachial plexus seen at the Mayo Clinic, Adson [267] found 73 per cent. in association with forceps delivery. Recovery to some degree occurred in practically every case. The greatest amount of recovery was experienced during the first three months. In some cases, improvement had continued over a period of twelve years. In the patients under 2 years of age, there was approximately one-third return of function; in those under 5 years, one-half return of function, and in those over 5 years the improvement progressed to about two-thirds normal function. Dislocations of the shoulder encountered seemed to develop rather after than during birth. That even total brachial paralysis at birth heals, generally without any disturbance, becomes evident from the publication of Froelich.[268]

Friedberg [269] recalls that chronic saturnism in childhood differs from that in the adult in that development is slower, colic is rare; characteristic blood findings are lacking, as is the gray gingival margin and there is an atypical localization of motor disturbances in the lower extremities. The difficulty of diagnosis is borne out by a case cited that

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265. Rosett, J.: Brain **45**:1 (June) 1922.
266. Neustädter, M.: New York J. Med. **22**:65 (Feb.) 1922.
267. Adson, A. W.: Northwest Med. **21**:33 (Feb.) 1922.
268. Froelich: Rev. de chir. **59**:419, 1921.
269. Friedberg, E.: Arch. f. Kinderh. **71**:25 (Feb.) 1922.

had escaped recognition for several years. With the elimination of the cause—playing with lead toys and lead types for years—the disturbance vanished.

Postdiphtheritic paralysis of the right pterygoid muscle and marked involvement of the second and third branches of the trigeminus nerve with recuperation have been reported by Huenerberger.[270] In a second patient, the muscles of neck and back were involved, the clinical picture resembling poliomyelitis. Labbe [271] was able to cure tardy diphtheritic paralysis by systematic treatment with antitoxin in seven children. In one child, the paralysis of the soft palate had been of four years' standing. Hallez [272] found lymphocytosis, hyperalbuminosis and hyperglycorachia in the cerebrospinal fluid of a girl of 12 suffering from postdiphtheritic paralysis.

Certain aspects of postdiphtheritic diaphragmatic paralysis are described by Mixsell and Giddings,[273] who report eight fatal cases occurring among 4,259 instances of diphtheria. In cases presenting involvement of the diaphragm, the mortality has been 100 per cent.

In a paper on infantile beriberi in the Philippines, Tupas [274] reports thirty-six cases, thirty of the patients being under 3 months old, the youngest 14 days, the oldest 1 year and 5 days old. The mortality was 30.5 per cent. The lesions in five cases examined postmortem were marked dilatation of heart, hydropericardium, punctate hemorrhages of lungs, congestion in various viscera and degenerative neuritis of the vagus nerve.

Erythroedema.—The disease described first in Australia by Swift (1914) in children as erythroedema, by Snowball as "raw beef hands and feet," and known in Sidney as "pink disease," has been observed repeatedly in this country, where the name acrodynia, as suggested by Weston (1920) is frequently used. Brown and Courtney with MacLachlan [275] discuss at length the complex clinical picture of this affection, which is considered a form of polyneuritis or radiculitis. The chief features are: nervous disturbances of sensory and trophic character; distressing paresthesias in fingers, feet and toes, leading to incessant scratching and rubbing; in some cases, diminished or absent cutaneous sensibility to pin pricks, and photophobia. The skin lesions are of greater value in the diagnosis, consisting in an erythematous eruption of almost edematous appearance, involving fingers and toes, and frequently extending to wrists and ankles. On the palms and soles, there is desquamation of "pin prick" character. There is excessive perspiration, and occasionally loosening and falling out of the teeth. Dulness and apathy alternate with restlessness. Anorexia and emaciation are present. Polymorphonucleosis is a symptom. There is a constant nasopharyngitis, on the subsidence of which, especially on removal of tonsils and adenoids, the children begin to improve. The seasonal incidence is suggestive of respiratory infections, including influenza as an etiologic factor, the syndrome probably being due to toxins. Eight observations are reported and the differential diagnosis is discussed.

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[270] Huenerberger, H.: Arch. f. Kinderh. **71**:175, 1922.

[271] Labbe, R.: Arch. de med. enf. **24**:612 (Oct.) 1921.

[272] Hallez: Presse méd. **29**:878, 1921.

[273] Mixsell, H. R., and Giddings, E.: Certain Aspects of Postdiphtheric Diaphragmatic Paralysis, J. A. M. A. **77**:590 (Aug. 20) 1921.

[274] Tupas, A. V.: Philippine Islands M. A. J., 1921, p. 108.

[275] Brown, A.; Courtney, A. M., and MacLachlan, I. F.: Arch. Pediat. **38**:609 (Oct.) 1921.

As Wood [276] has notes on eighty-eight cases, the disease seems to be not uncommon in Australia.

Zahorsky [277] pleads for the adoption of the original term erythredema as used by the Australian physicians, especially since there is no identity with the great epidemics of acrodynia in Paris at the beginning of the last century. He observed pronounced atrophy of the muscles in one of his seven cases. In another, there were large areas of anesthesia; and in two babies, voluntary movements of both lower extremities ceased completely for several weeks. Field [278] presents a typical case in an 18 months old baby and states that about 100 cases have been reported to date. Mutilations and ulcerations, namely loss of finger tips due to gangrene, and chronic ulcers in each sole, from which, as from the nasal discharge, a diphtheroid bacillus was cultivated, have been reported by Weber.[279] Thursfield and Paterson [280] describe a case under the title dermatopolyneuritis, presenting signs of neuromuscular lesions with extreme hypotonia. An example is cited by Miller [281] under the name of "polyneuritic syndrome," and a doubtful case in which bronchiectasis is credited with the same relation to erythrodema as the nasal infections in some of the reported cases is described by Davis.[282]

Vipond,[283] from the study of two instances, concludes that the nose cavity is the point of inoculation, as a discharge is the first sign. Then follows general adenopathy pointing to a generalized infection. The next symptoms to be observed are the characteristic findings on hands and feet, these being of vasomotor nature. He obtained a gram-positive diplococcus from the material aspirated from an enlarged lymph gland. Vaccine prepared from this micro-organism had in both instances splendid results.

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[276] 276. Wood, A. J.: M. J. Australia **1**:145 (Feb. 19) 1921.

[277] 277. Zahorsky, J.: Semeiology of Pink Disease (Erythredema, Acrodynia), J. A. M. A. **79**:1975 (Dec. 9) 1922; Missouri M. A. J. **19**:296 (July) 1922.

[278] 278. Field, M. C.: Arch. Pediat. **39**:116 (Feb.) 1922.

[279] 279. Weber, F. P.: Brit. J. Dis. Child. **19**:17 (Jan.-March) 1922.

[280] 280. Thursfield, J. H., and Paterson, D. H.: Brit. J. Dis. Child. **19**:27 (Jan.-March) 1922.

[281] 281. Miller, M. K.: Indiana M. A. J. **14**:144 (May) 1921.

[282] 282. Davis, Clara M.: Arch. Pediat. **39**:611 (Sept.) 1922.

[283] 283. Vipond, A. E.: Arch. Pediat. **39**:699 (Nov.) 1922.

SPASMOPHILIA; INFANTILE TETANY

Nassau [284] distinguishes two different types of tetany. 1. The early form, which occurs in the first three months. It is initiated by eclamptic attacks and other signs, such as the positive facial phenomenon. Kathodic overirritability may follow after an interval of up to 18 days. 2. The later form, which occurs in the second semester of life and is characterized by the frequency of laryngospasm as the initial symptom of manifest tetany. A predisposition for edema seems to be characteristic of spasmophilia and may occur in both types. In the eclamptic form, rapidily passing changes, oscillations in the "milieu interne" seem to play an important rôle, and in the laryngospastic form, possibly avitaminosis. The disturbance of salt metabolism is the common symptom; in the early form, an exaggerated retention of sodium and potassium in contrast to calcium, in the later type, a decreased retention of calcium being present.

A horse shoe shaped depression of the cornea during eclamptic attacks was observed by Ochsenius,[285] possibly caused by reduction of the intra-ocular tension.

Lemair and Olivier [286] aver that tetany in the infant may cause gastrospasm or pylorospasm, manifesting itself in habitual vomiting, which yields rapidly to the classic antitetany treatment.

Moschini [287] describes three cases of bronchotetany with necropsy findings. The importance of the recognition of this condition is evident, as antitetany measures would attenuate or cure bronchotetany.

The view expressed by Escherich and Ibrahim that the cause of sudden death among spasmophilic children is heart tetany lately found support in Koplik's [288] observations of bradycardia during attacks of sudden apnea. The author declares this symptom pathognomonic of spasmophilia. On the other hand, in the case reported by Iwabuchi,[289] marked pathologic changes in the vagus nucleus are described as the possible cause of death.

Among 1,648 schoolchildren examined by Schulze,[290] Chvostek's sign was present in 139 cases. As more than two-thirds of these were

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284. Nassau, E.: Ztschr. f. Kinderh. **28**:310 (April) 1921.
285. Ochsenius, K.: Monatschr. f. Kinderh. **21**:151 (May) 1921.
286. Lemair, H., and Olivier, M.: Nourisson **10**:305 (Sept.) 1922.
287. Moschini, C.: Policlinico (sez. prat.) **28**:1616 (Nov. 28) 1921.
288. Koplik, H.: Arch. Pediat. **39**:504 (Aug.) 1922.
289. Iwabuchi, T.: Ztschr. f. Kinderh. **33**:223 (Aug.) 1922.
290. Schulze, A.: Monatschr. f. Kinderh. **22**:484, 1921.

to be considered as spasmophilic, the author concurs in the opinion of those who declare the facial phenomenon at this age at least as extremely suspicious of latent spasmophilia. Mosse,[291] on the basis of clinical observations and the fact that his determinations of calcium, phosphorus and the bicarbonate of blood serum revealed no differences between the groups of children with and without facial sign, comes to the opposite conclusion.

Myographic curves taken by Bossert and Gralka[292] in twenty-two children suffering from various signs of spasmophilia are interpreted as indicating that in infantile tetany (in the strict sense) calcium deficiency, possibly due to dysfunction of the parathyroids, entails imbibition of the musculature, altering its contractibility and resulting in carpopedal spasms, and that in the group of babies with laryngospasm as the cardinal symptom there exists an extreme overirritability of the nervous system referable to a prevalent calcium deficiency in the nerve tissue; that in eclampsia it is the prevalence of calcium deficiency in the brain especially that is to be held the responsible factor.

The influence of sodium and potassium phosphates on normal and spasmophilic infants has been studied by a number of authors. In numerous experiments conducted by Jeppsson,[293] administration of kalium and natrium phosphate provoked increased galvanic and mechanic irritability, typical laryngospasm and, in one child, typical tetany. In one experiment, dangerous expiratory apnea appeared. In dogs and rabbits, galvanic and mechanical overexcitability, eclamptic convulsions and tetany spasms and respiratory spasms, mostly of the character of laryngospasm, could be produced. The effects of the alkali phosphates was not due exclusively to the one or the other of their ions. Whey freed of its phosphates failed to increase the irritability.

Artificial mixtures of the salts approximately as they are present in cow's milk increased the tendency to spasmophilia, in the experiments of Wernstedt,[294] by disturbing the salt metabolism, and Roemer[295] demonstrated the tetanigenous effect of the basic sodium phosphate. On the other hand, Calvin and Borovsky[296] were unable to obtain the results of Jeppsson; and Wetzel[297] is convinced that the kalium ion as

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291. Mosse, K.: Jahrb. f. Kinderh. **99**:244 (Sept.) 1922.

292. Bossert, O., and Gralka, R.: Jahrb. f. Kinderh. **94**:145, 1921.

293. Jeppsson, K., and Klercher, K. O.: Ztschr. f. Kinderh. **28**:71-167 (March 21) 1921.

294. Wernstedt, J. W.: Acta Pediat. **1**:133 (June) 1921; **1**:257 (Dec.) 1921.

295. Roemer, P.: J. de med. de Paris **41**:647, 669, 1922.

296. Calvin, J. K., and Borovsky, M. P.: Results Following Administration of Alkali Phosphates to Spasmophilic Rachitic and Normal Infants, Am. J. Dis. Child. **23**:238 (March) 1922.

297. Wetzel, A.: Ztschr. f. Kinderh. **32**:105 (March) 1922.

such has no spasmogenic action and that the untoward effect of cow's milk on spasmophilia is not to be ascribed to the larger amount of kalium ions in comparison to that in human milk.

The association of tetany with lowered calcium in the blood has received attention by Kramer, Tisdall and Howland,[298] who regularly found the calcium of the serum diminished in active tetany. They conclude that the increased irritability is due to the diminished concentration of calcium in the serum or in the ratio $\frac{Ca + Mg}{Na + K}$, the stimulating effect of the sodium and potassium being unopposed by the inhibitory effect of calcium. Thiemich's sign in older children, however, according to von Meysenburg,[299] is not based on lowered blood calcium.

That hyperphosphemia is an important symptom, possibly one of the causative factors in tetany, is believed by Elias and Spiegel,[300] who found the inorganic phosphorus content in the serum characteristically increased in tetany.

A number of authors assume that alkalosis is the underlying factor in tetany; and recently it was discovered that guanidin may provoke the syndrome without any relationship to calcium deficiency. Grant [301] records symptoms of tetany following an overdosage of sodium bicarbonate, which upset the ratio of sodium bicarbonate to carbonic acid in the blood. Tetany in gastric obstruction is declared to be due to an excess of sodium bicarbonate, resulting from the fact that it is impossible for the secreted hydrochloric acid to pass into the intestines to stimulate the flow of alkaline intestinal secretion. Goldmann [302] again reports eleven cases of bicarbonate tetany due to hyperpnea, with consequential alkalosis through excessive reduction of carbon dioxid. In the cases of Barker and Sprunt [303] and of Haas,[304] the tetany attacks were caused by hyperpnea in epidemic encephalitis. Freudenberg and György [305] come to the conclusion that the alkalosis existing in manifest tetany acts by altering the blood content of active calcium (dissociation of blood calcium), and that guanidin acts by displacing the calcium in the colloids. Consequently, they treat active tetany with "acidotic" remedies, that

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298. Kramer, Benjamin; Tisdall, F. F., and Howland, James: Infantile Tetany, Am. J. Dis. Child. **22**:431 (Nov.) 1921.

299. Von Meysenburg, L.: Studies in Spasmophilia; Blood Calcium and Calcium Therapy in Older Children with Thiemich's Sign, Am. J. Dis. Child. **21**:150 (Aug.) 1921.

300. Elias, H., and Spiegel, E. A.: Wien. Arch. f. inn. Med. **2**:447 (June) 1921.

301. Grant, S. B.: Tetany, Arch. Int. Med. **30**:305 (Sept.) 1922.

302. Goldmann, Alfred: Clinical Tetany by Forced Respiration, J. A. M. A. **78**:1193 (April 22) 1922.

303. Barker, L. F., and Sprunt, T. P.: Endocrinology **6**:1 (Jan.) 1922.

304. Haas, S. V.: Arch. Pediat. **38**:785, 1921.

305. Freudenberg, E., and György, P.: Klin. Wchnschr. **1**:222 (Jan. 28), 410 (Feb. 25) 1922; Jahrb. f. Kinderh. **96**:5, 1921.

in the metabolism tend to increase acidity, such as hydrochloric acid milk, introduced by Scheer,[306] and "salmiak" (ammonium-chlorid), which Haldane[307] proved to produce in man marked and prolonged acidosis by lessening the alkali reserve. The results were excellent, apparently proving the correctness of the premises. However, Jones and Nye[308] and Calvin and Borovsky[309] dispute the theory of alkalosis in tetany.

Coda[310] and other authors incriminate the endocrine system, which may act on the vegetative nervous system, the calcium metabolism, the so-called myoneural conjunction or all these factors.

As regards the pathogenesis of the type of tetany following parathyroidectomy, the experiments made on dogs by Dragstedt[311] and Luckhardt and Rosenbloom[312] indicate that it is due to toxic substances chiefly derived from the gastro-intestinal tract through the activity of proteolytic bacteria, most probably of the nature of amins. The function of the parathyroids is to prevent this intoxication; and dogs may be kept alive indefinitely after parathyroidectomy, if by certain means this toxemia of intestinal origin is prevented.

The investigations of Hess[313] of New York with Gutman, and of Hess and Unger[314] demonstrated that, in infants, the inorganic phosphorus of blood can be raised to the normal level by exposures to the sun's rays or to the carbon arc lamp. This fact and the marked seasonal variations in the sun's spectrum prompted investigations by Hess and Lundagen,[315] which demonstrated a seasonal tide of blood phosphate during the spring and summer, the dominating factor being the sun light. Hess associated these facts with the peak of tetany and with rachitis.

GENERAL CONVULSIONS

That there exists a predisposition to convulsions separate from spasmophilia, that eclampsia and tetany have not the close relationship generally assumed is the contention of Goett and Wildbrett,[316] who

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306. Scheer, K.: Jahrb. f. Kinderh. **97**:130 (Feb.) 1922.

307. Haldane, J. B. S.: J. Physiol. **55**:265 (Aug.) 1921.

308. Jones, M. R., and Nye, L. L.: J. Biol. Chem. **47**:321 (July) 1921.

309. Calvin, J. K., and Borovsky, M. P.: Spasmophilia and Alkali Reserve, Am. J. Dis. Child. **23**:493 (June) 1922.

310. Coda, M.: Pediatria **30**:764 (Aug. 15) 1922.

311. Dragstedt, L. R.: Pathogenesis of Parathyroid Tetany, J. A. M. A. **79**:1593 (Nov. 4) 1922.

312. Luckhardt, A. B., and Rosenbloom, P. J.: Science **56** (July 14) 1922; Proc. Soc. Exper. Biol. & Med. **19**:129, 1921.

313. Hess, A. E., and Gutman, P.: Proc. Soc. Exper. Biol. & Med. **19**:31, 1921.

314. Hess, A. F., and Unger, L. J.: Use of Carbon Arc Light in Prevention and Cure of Rickets, J. A. M. A. **78**:1596 (May 27) 1922.

315. Hess, A. F., and Lundagen, M. A.: Seasonal Tide of Blood Phosphate, J. A. M. A. **79**:2210 (Dec. 30) 1922.

316. Goett and Wildbrett: München. med. Wchnschr. **69**:884, 1922.

found that babies of families in whom there exist lefthandedness, various spasms or genuine epilepsy are predisposed to eclampsia.

An interesting problem as to the pathogenesis of convulsions in early childhood is involved in the observation of Reiche[317] of an apparently primarily increased chlorid concentration in the cerebrospinal fluid, causing, according to the law of osmosis, an increase of the quantity of the spinal fluid, and thus also of the intraspinal pressure, with consequent convulsions, in a baby, 1 year old.

The importance of reflex irritation as a cause of convulsions has been undoubtedly exaggerated. Morse[318] never saw convulsions due to phimosis, eye strain, teething or worms, etc.; with the exception of one case in which convulsions ceased after administration of an anthelmintic, and another case in which the seizures ceased after stretching of the sphincter ani by a quack doctor. However, in convulsions following eating of indigestible and improper food, reflex irritation seems more important than toxic absorption.

The treatment of convulsions, especially of spasmophilic nature, has been outlined by Blühdorn.[319] That epilepsy as a disease is not transmitted from parent to offspring but rather indicates a nervous system lacking in normal stability is the belief of Thom and Walker.[320] The manifestations of this instability may be mental deficiency, insanity, neurologic and psychopathic disorders and convulsions from various exciting causes that would have little or no effect on a normal nervous system. The statistics of Burr[321] point likewise to an indirect, general, nonspecific inheritance.

Antheaume and Trepsat[322] produced violent convulsions, followed by death, in several rabbits by injecting the serum of an epileptic.

That jacksonian epilepsy in a large percentage of cases does not mean a definite focal disease of the cortex is emphasized by Wilson,[323] who enumerates various conditions, some remote from the cortex, that are occasionally associated with monospasms or hemispasms. Probably, the commonest cause of this form of spasm is idiopathic epilepsy itself ("idiopathic epilepsy with inside jacksonian spasm"). A person with this type should, therefore, not be operated on unless other symptoms of intracranial disease are present.

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[317] Reiche, F.: München. med. Wchnschr. **68**:202, 1922.

[318] Morse, J. L.: Convulsive Disorders of Childhood, J. A. M. A. **78**:175 (Jan. 21) 1922.

[319] Blühdorn, K.: Med. Klin. **18**:733 (June 4) 1922.

[320] Thom, D. A., and Walker, G. S.: Am. J. Psychiat. **1**:613 (April) 1922.

[321] Burr, C. W.: Heredity in Epilepsy, Arch. Neurol. & Psychiat. **7**:721 (June) 1922.

[322] Antheaume, A., and Trepsat, L.: Encéphale **17**:103 (June) 1922.

[323] Wilson, George: Diagnostic Significance of Jacksonian Epilepsy, J. A. M. A. **76**:842 (March 26) 1921.

Jacksonian epilepsy, with attacks in the left arm, in a girl of 4 was completely cured following treatment for ascaris. Sironi,[324] who reports this case, theorizes that the toxins of the helminths may have acted on a focus of lesser resistance, perhaps a residue of a previous infection in the brain.

The investigations of reflex epilepsy found a real basis in the striking results of animal experiments conducted by Amantea,[325] who, by cutaneous stimulations, especially in the so-called reflexogenic areas, succeeded in eliciting epileptic seizures.

Theories as to the pathogenic relation of the so-called pyknoleptic attacks or Friedmann's disease are dealt with by Meyer.[326] These "repeated minor seizures" resemble petit mal in some respect, but not in others, as the children remain mentally normal; ordinary antiepileptic measures have no effect; the attacks cease as a rule toward puberty, and the prognosis is favorable. During an attack, there is a sudden and short suspension of the higher psychic functions, a sudden interruption of the occupation and rolling of the eyes. After from one-quarter to one-half minute, the attack subsides, and the occupation is continued. He reports four cases, in children from 7 to 12 years of age with an inherited nervous taint, but bright and lively. The seizures occurred up to thirty times a day, lasting from one-quarter to one-half minute. While some authors consider the affection a form of epilepsy with intact mentality, Meyer classifies it as a special group of the neuropathic forms of reactions, entirely apart from epilepsy or hysteria. Physical fatigue seemed to elicit the manifestations. He recommends calcium up to 6 gm. a day, with small doses of phenobarbital (luminal).

Stargardter,[327] who describes the pictures of pyknolepsy in four children, and Husler,[328] who presents a monograph on the clinic of epileptiform affections in children, see the pathogenic basis of these "multiple absences" in marked neuropsychopathy. On this basis, these simple and uniform seizures develop together with other neuropathic manifestations. One of the cases of Stargardter demonstrates that pyknolepsy may grow also on the basis of true epilepsy. Caffein proved efficacious in the treatment.

Deep unconsciousness, spasms, nocturnal character, falling with injuries, the onset of the attacks before the fifth year of life, exhaustion and the therapeutic effect of phenobarbital would, in the experience of Stier,[329] render the seizures suspicious of being true epilepsy and thus make the prognosis more serious.

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324. Sironi, L.: Pediatria **29**:397 (May 1) 1921.

325. Amantea, G.: Arch. f. d. ges. Physiol. **188**:287, 1921; Policlinico (sez. prat.) **27**:462, 1920.

326. Meyer, M.: Ztschr. f. Kinderh. **27**:293 (Jan.) 1921.

327. Stargardter, J.: Jahrb. f. Kinderh. **95**:230, 1921.

328. Husler, J.: Ergebn. d. inn. Med. u. Kinderh. **19**:652, 1921.

329. Stier, E.: Ztschr. f. ges. Neurol. u. Psychiat. **80**:143, 1922.

Tests of the oculocardiac reflex, made by Rubinovitch and Chavany,[330] in fifty-eight epileptics, revealed that in 62.5 per cent. of the cases, the bradycardia was followed by tachycardia for a minute. They see in this fact a new means for the differential diagnosis in doubtful cases.

Phenobarbital or sodium phenobarbital has found a widespread therapeutic use in epilepsy, and is considered by most authors the most effective symptomatic remedy, reducing decidedly the number and severity of the convulsions. No mental deterioration nor any toxic or accumulative by-effects were observed by Grinker[331] and I. J. Sands.[332] However, with the discontinuation of its administrtation, the seizures returned often at more frequent intervals and with greater intensity. As the remedy has no action in hysteria crises, Maillard[333] considers it an aid in the diagnosis.

Cheinisse,[334] on the other hand, warns that, though the drug acts well in the seizures, it also checks the normal activity of the nerve centers, entailing a physical and mental torpor. He cites Ducoste, who combines the drug with belladonna or caffein to ward off these by-effects, and mentions other authors who recorded negative therapeutic results and saw death in status epilepticus following sudden suspension of phenobarbital treatment. Weber[335] and Fremel, with Herschmann,[336] write on phenobarbital by-effects. The latter authors emphasize injuries to the cerebellar and vestibular system and comment on barbital psychosis.

Fischer[337] advances evidence that the capacity of the body to react with convulsions has a central and peripheral component, the latter having a relationship especially to the suprarenals. Diminution of their substance by extirpation is followed by reduction of convulsive reactions on stimulation. Enlargement of the suprarenal cortex as by castration or alcohol poisoning of rabbits, is followed by an increase of the spastic reaction.

Acting on this principal, Steinthal[338] operated on eleven epileptics, extirpating one of the suprarenals, but without convincing results.

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330. Roubinovitch, J., and Chavany, J. A.: Bull. Acad. de med. **85**:687 (June 7) 1921.

331. Grinker, J.: Phenobarbital in Epilepsy, J. A. M. A. **79**:788 (Sept. 2) 1922.

332. Sands, I. J.: Luminal Therapy in Epileptic Seizures, Arch. Neurol. & Psychiat. **5**:305 (March) 1921.

333. Maillard, G.: Bull. med. **35**:769, 1921.

334. Cheinisse, L.: Presse méd. **30**:42 (Jan. 14) 1922.

335. Weber, H.: Therap. Halbmonatsch. **35**:467 (Aug. 1) 1921.

336. Fremel, F., and Herschmann, H.: Med. Klin. **17**:716 (June 12) 1921.

337. Fischer, Heinrich: Deutsch. Ztschr. f. Nervenh. **71**:116, 1921.

338. Steinthal, C.: Zentralbl. f. Chir. **48**:878 (June 25) 1921.

Sándor [339] obtained in four cases a certain degree of benefit, which, on account of the short postoperative period, cannot be determined yet. Fischer [340] reports distinctive improvement in a case of long standing, and Kersten [341] in two epileptics.

Sultan [342] holds the prospects of a cure by this operataion as small, and still more skeptical is Specht,[343] who, from experimental research, denies justification of surarenalectomy in treatment of epilepsy.

PSYCHOLOGY

The biography of an infant prodigy, Chr. H. Heineken, born at Luebeck, 200 years ago, has been sketched by Brüning.[344] At the age of 14 months, he knew the whole Bible; at 2½ years, ancient history, geography, anatomy and 800 Latin words, learning weekly over 150 new vocables. He could read German and Latin and spoke German, low German, Latin and French perfectly. When 3 years old, he could add, subtract and multiply, and in his fourth year he learned 220 songs, eighty psalms, 1,500 verses and sentences of Latin writers. Shortly before his death, at the age of 4 years and 4 months, he studied astronomy.

Mosse,[345] when testing children in the kindergartens, encountered suggestibility at the early age of 3 years. Experiences at the dispensary demonstrated that the results of examinations of healthy children as to their suggestibility are not applicable to the sick child, since the suggestibility of the former decreases, that of the latter increases with age. The great suggestibility of children necessitates great caution in children's testimonies at law suits.

Among 70,555 school children of Vienna examined, Neurath [346] found lefthandedness existing in 3.85 per cent. His studies lead him to the conclusion that it is a congenital peculiarity, more frequent in the male than in the female, inherited directly, usually from the mother. Not only the left hand, but the total motor innervation area of the right hemisphere, as to skilfulness and spontaneous motility revealed a psychomotor preponderance and superiority over the right side of the body. The combination with disorders of speech is not infrequent. The lefthanded persons represent not a type of degeneracy, but a variety of the human species, inherited from generation to generation. In pedagogic practice, the author postulates for the sinistrals a wide range of liberty.

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339. Sándor, S.: Zentralbl. f. Chir. **48**:881 (June 25) 1921.
340. Fischer, H.: Ann. Surg. **76**:176 (Aug.) 1922.
341. Kersten, H.: Med. Klin. **49**:1553 (Dec. 3) 1922.
342. Sultan, C.: Deutsch. med. Wchnschr. **48**:153 (Feb. 2) 1922.
343. Specht, O.: Beitr. z. klin. Chir. **125**:347, 1922.
344. Brüning, H.: Monatschr. f. Kinderh. **22**:230 (Nov.) 1921.
345. Mosse, K.: Ztschr. f. Kinderh. **27**:65, 1922.
346. Neurath, R.: Wein. klin. Wchnschr. **35**:895, 1922.

Sieben[347] analyzes sinistrality in five generations, and an editorial in *The Journal of the American Medical Association* dealing with this condition,[348] quotes C. Quinan as finding that among sinistrals stammering is three to six times more frequent than among dextrals.

SEXUALITY

That the conception of asexuality or presexuality in childhood is not tenable, becomes evident from the abundant material collected by Freud and his school. Friedjung[349] insists that the scope of sexual manifestations embrace not only instinct acts aiming directly at heterosexual union, but also pleasurable gratifications of Freud's so-called partial instincts, such as olfactory impulses and masochistic and sadistic tendencies. The earliest period of childhood is characterized by autoeroticism, originating in various erogenous zones, especially the lips, skin, anus and urethra. Cases of enuresis were traced to urethral eroticism. There is no escape for the child from experiencing sensations localized in the sexual organs, either by spontaneous erections which may occur very early or by the necessary washing processes. Masturbation has been observed in infants of 9 and 13 months. Among the manifestations of hetero-eroticism, the most frequent is seeking after and playing with the breast of the mother or some loved woman with excitement, observed in boys from the second to the fourth year of life; obviously passionate kissing of the naked arm or neck of adults, excitement displayed when seeing nude legs and other more aggressive acts. Naturally, sexual curiosity is early focused on the genitals, in particular of the opposite sex, and may lead to mutual exhibition and some more aggressive acts. The habit of adults of taking the child into their bed is very deleterious, and mothers are often alarmed at the behavior of their little boys. In a chapter on psychosexual conduct, Friedjung cites examples of the Oedipus complex, exhibition and curiosity. Morbid modesty at puberty had in some instances its source in fear to have onanism detected. It is significant that all conditions mentioned fall within the normal, and that the children offered later no deviations from the average.

There exists a false incontinence of the sphincters in children due to what Morichau and Beauchant[350] term paragenital auto-eroticism. They hold the urine or stool back on account of a pleasurable sensation then felt in the bladder, urethra or anus until this voluntary retention is overcome by the demands of Nature and the child soils his clothing.

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347. Sieben, W.: Deutsch. Ztschr. f. Nervenh. **73**:213, 1922.

348. Is Lefthandedness a Sign of Inferiority? Editorial, J. A. M. A. **76**:1010 (April 9) 1921.

349. Friedjung, J. K.: Ztschr. f. Kinderh. **31**:1, 1921.

350. Morichau-Beauchant, R.: Paris méd. **12**:83 (July 22) 1922.

Bed wetting existing in a youth of 18 since his seventh year of life had been an unconscious equivalent for a sexual act. This was brought out through the psychanalysis by Herbert,[351] and is in line with Freud's statement that in infancy excretory functions (urinary and alvine) are charged with a sexual tone.

Three interesting cases, in two boys and a girl, from 3½ to 5 years old, reported by Klaesi,[352] demonstrate how marked an imprint of sublimated spirituality the sexual life at this age may have and how, under certain conditions, it may assume the qualities of virtue, as modesty, devotion, self-sacrifice, chivalry and courage, as in the adult. The author explains that whether in such cases it comes to masturbation or intercourse or not depends merely on external circumstances, and such acts are not necessarily to be considered as diagnostic signs of psychopathy.

There is no doubt that, as Anton [353] states, pathologic instances of precocious puberty with signs of accelerated physical and mental development, are not rare. He quotes Meynert's experience that powerful impressions and experiences even in early age may become fixed, laying the foundations for perversities and sexual excitations that subjugate the nervous system to the instincts and render the emotional life morbid. Great caution is necessary in the selection of persons to educate children.

Obstinate onanism since earliest childhood in a girl of 10, observed by Ellison,[354] was cured through fear of a threatened operation on the genitals after admission to a hospital.

NEUROPSYCHOPATHIC DISORDERS

Two principal groups of psychic anomalies in early childhood are distinguished by Goett; [355] (1) defects in the intellectual sphere; oligophrenia, and (2) the psychopathic anomalies. The latter are within the field of emotions, volition and character; within the personality proper. The earliest sign may be dysthymia and cyclothymia. The active subform is characterized by exaggeration of the instinct of self-preservation, manifesting itself in egoism; the passive type, by the prevalence of phantastic dreaminess and brooding logic in comparison to the pleasures of the senses of the normal child. Not the adult but the healthy child of the same age must be the standard in determining what is normal or abnormal, and the boundary of normality should be widely drawn. Psychopathy must not be confounded with naughtiness. In the psychopathic child, the egoistic tendencies are unrestrained for

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351. Herbert, S.: Psychoanalytic Rev. **9**:263, 1922.
352. Klaesi, J.: Ztschr. f. ges. Neurol. u. Psychiat. **74**:362, 1922.
353. Anton: Ethik. Paedagogik u. Hyg. d. Geschlechtslebens **1**:10, 1922.
354. Ellison, E. M.: New Orleans M. & S. J. **74**:160 (Sept.) 1921.
355. Goett, T.: Klin. Wchnschr. **1**:265, 1922.

lack of inhibition, rooted in its unfortunate "anlage." In the non-psychopathic, merely spoiled child, the egoism is unbridled because there exists no necessity for restraint.

Increasing attention is given to nervous disorders as the result of injurious environment, especially of the influence of persons around the child. A characteristic type is circumscribed as the "only child." Friedjung[356] observed among 264 "only children" not more than thirty-five that were healthy. Other types are the favorite children, such as the first born, or the late born child, the only boy among several sisters or vice versa. While these children suffer from exaggerated care, another group suffers from the opposite: such as the child that is not loved, that is among strangers, the foster child, the child that is less beautiful or talented, etc.

The importance of the development of the right kind of emotions by young persons and their correct guidance by the parent is emphasized by Williams.[357]

The polymorphous clinical picture in the nervous child is analyzed by Heubner[358] and exemplified by a number of instructive cases from his vast experience. The essential feature is the predisposition of the nervous system to react in an abnormal manner to the common stimulations of life. The nervous child often suffers from anorexia, pallor and headache. The pallor is not due to any hematologic anomaly but to a vasor disturbance; the headache can be traced mostly to a provocative cause; the anorexia may find its explanation in the lack of pleasure children, at least in the playing age, find in eating. Other manifestations are vomiting, abdominal pain, sleeplessness, enuresis, masturbation and nervous disturbances of the respiratory organs and the heart, and finally tics and similar motor disturbances. They all are discussed.

Many symptoms of so-called neuropathic diathesis may be due to anaphylactic reaction to food proteins. This is brought out by Shannon,[359] who, in eight cases of neuropathic diathesis in infants and children, proved protein sensitization by cutaneous tests made with a number of foods. All showed definite relief from nervous symptoms after exclusion of the offending food or following specific protein therapy.

Delinquency with its characteristic lack of self-control, of moral and ethic motives, loss of well-balanced, regulated conduct and of social adaptation, as again pointed out by Cimbal,[360] has its origin mostly in extraneous factors, such as lack of home and school education and demoralizing conceptions, though even an orderly home environment offers no absolute protection. Its manifestation at school age is mostly truancy; later theft and fraud, and at puberty a craving for stimulations by tobacco, exciting reading and shows and vagabondage. Mental deterioration may supervene, with impairment of memory, sometimes surpassing that of paralysis, when the distinction from juvenile insanity may be difficult. Predisposing factors are congenital inferiority and exhaustion of the nervous system.

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[356] Friedjung, J. K.: Wien. klin. Wchnschr. **34**:70 (Feb. 17) 1921; Deutsch. med. Wchnschr. **47**:949 (Aug. 18) 1921.

[357] Williams, T. A.: Arch. Pediat. **39**:180 (March) 1922.

[358] Heubner, O.: Klin. Wchnschr. **1**:980 (May 13) 1922.

[359] Shannon, W. R.: Neuropathic Manifestations as a Result of Anaphylactic Reaction to Foods Contained in Their Dietary, Am. J. Dis. Child. **24**:89 (July) 1922.

To decide how far an innate mental anomaly and how far the child's environment is responsible for abnormal conduct reactions, Lurie [361] urges that the child be taken out of that environment and placed in a psychopathic institution especially fitted for such scientific observations.

Sundell [362] believes that sleeplessness in infants often has its cause in the nursery, especially in an irregular bed time and excitement while awake. These and other educational errors must be avoided. Hypnotics must be reserved for exceptional occasions, and then an adequate dose should be given for the first evening, a gradually lessened dose for the next two days and the fourth evening the hypnotic should be omitted. The various sedative and soporiferous remedies employed in childhood were the subject of an instructive paper by Rominger.[363]

De Haan [364] presents arguments that the main cause of enuresis is exceptionally profound sleep. All that is necessary to cure it is to render this sleep less profound at night by a nap during the day or by putting the child to bed a few hours earlier than usual, but without darkening the room till the usual time. In addition to this procedure, Zappert [365] recommends life in the country, psychotherapy reeducation of the bladder and reduction of sodium chlorid in the diet. Also potatoes, bread and vegetables should be lessened in quantity as they cause an increased output of potassium with a postponed elimination, taking place during the night, resulting in nycturia, polyuria and pollakiuria.

MIGRAINE

That migraine is not rare in children is the experience of Comby.[366] The hereditary predisposition is homologous and heterologous, since asthma, neuropathies, hysteria and arthritism may be traced in the ancestry; and the children themselves later may have neuroarthritic manifestations, such as asthma, diabetes, renal calculi or gout.

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[360] Cimbal, W.: Deutsch. Ztschr. f. Nervenh. **68-69**:365, 1921.

[361] Lurie, L. A.: Treatment of the Subnormal and Psychopathic Child, J. A. M. A. **71**:1386 (May 21) 1921.

[362] Sundell, C. E.: Practitioner **109**:89 (July) 1922.

[363] Rominger, E.: Klin. Wchnschr. **1**:1949 (Sept. 23) 1922

[364] De Haan, P. B.: Nederl. Tijdschr. v. Geneesk. **2**:1666 (Oct. 1) 1921; abstr., J. A. M. A. **77**:2154 (Dec. 31) 1921.

[365] Zappert, J.: Klin. Wchnschr. **1**:27 (Jan. 1) 1922.

[366] Comby, J.: Arch. de méd. d. enf. **24**:29 (Jan.) 1921.

Curschmann[367] saw migraine as early as in the beginning of the second year of life. During school age, the affection is characterized by its association with abdominal symptoms of splanchnogenic origin. Navel colic, many cases of supposed appendicitis, of gastric or duodenal ulcers, etc., have been really attacks of migraine or its equivalent. There may even be fever present. The splanchnogenic origin of the abdominal pains becomes apparent from the paroxysmal rise of blood pressure. A number of instructive case histories illustrate the various clinical pictures. Anaphylactic shock and spasmophilia or parathyroid states seem sometimes to coexist. Specific antitetany remedies, such as calcium, prove of great benefit.

Certain gastralgias in the adult in connection with migraine, either accompanying the typical attacks or being of the vicarious or the larval, irregular type, have long been known. Only recently, Brams[368] has reported a number of his observations at the policlinic of Paul Cohnheim in Berlin; and in one of the seven cases with periodical abdominal crises, cited by Buchanan,[369] the patient had been operated on but no lesion was discovered.

That such epigastric pains are related to migraine and hypertension due to vascular spasms seems very probable from the experiences of Hadlich[370] that migraine and hypertension frequently occur in one and the same patient; or that hypertension exists in one and migraine in another member of the family.

It seems noteworthy that systematic ingestion of peptone before each meal and Bonche's method of weekly injections of horse serum or crotalin proved useful in certain cases of migraine as reported by Pagniez.[371] Loewenthal[372] saw beneficial results from treatment with radium emanations, and Sicard[373] and his co-workers noticed that following systematic injections of sodium carbonate, the migraine ceased in every instance.

PSYCHIC DEFECTS

Psychometric examinations made by Raeder[374] of twenty-two children of syphilitic parents showed psychic terracing pari passu, with the

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367. Curschmann, H.: München. med. Wchnschr. **69**:1747 (Dec. 22) 1922.

368. Brams, W. A.: Abdominal Migraine, J. A. M. A. **78**:26 (Jan. 7) 1922.

369. Buchanan, J. A.: J. Nerv. & Ment. Dis. **54**:406 (Nov.) 1921.

370. Hadlich: Deutsch. Ztschr. f. Nervenh. **75**:125, 1922.

371. Pagniez, P.: Presse méd. **29**:45 (Jan. 15) 1921.

372. Loewenthal, S.: München. med. Wchnschr. **67**:971 (June 30) 1922.

373. Sicard, J. A., Parafand, Forestier: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:1204 (July 22) 1921; abstr., J. A. M. A. **77**:1052 (Sept. 24) 1921.

374. Raeder, O. J.: Feeblemindedness in Hereditary Neurosyphilis, Am. J. Dis. Child. **21**:240 (March) 1921.

grades of physical defects. The virulence of the congenital syphilis toxin in a given family of children, as evidenced by psychometric analysis and biochemical tests, varied inversely with the order of birth.

There is evidence accumulating that an acquired iodiocy of parathyroid origin is not uncommon. Comby[375] states that fortunately these cases are amenable to parathyroid treatment.

Gordon[376] found lefthandedness in 18.2 per cent. of children in schools for the mentally defective. It was often associated with defects of speech. The explanation given is that something had occurred interfering with proper functioning of the dominant hemisphere, the same cause affecting the higher intellectual centers, assumed to be localized in the same hemisphere. Mirror writing was more often encountered than in pupils in public schools.

True mental disease is extremely rare in childhood. Excluding postinfectious mental disturbances, juvenile paresis, epileptiform phenomena, psychoneurosis, constitutional psychopathy and mental defectiveness, only eighteen instances of true psychosis in 5,000 hospital admissions were observed by Strecker[377] in children under 15 years of age. Four were of indeterminable character; in ten the diagnosis was manic-depressive psychosis, in four dementia praecox. The symptomatology is essentially more simple in children than in the adult, presenting elementary emotional reactions and trivial delusions. Alexander is quoted as stating that between 10 and 30 per cent. of psychoses in children are due to acute infectious diseases, especially exanthemas, and recently also epidemic encephalitis.

Schnabel's[378] review of 231 cases of psychic disturbances at the ages of from 2 to 16 years, observed at the psychiatric clinic at Zürich, demonstrates the good prognosis of hysteria. Then follow the constitutional psychoses, the psychopathic conditions and moral defectiveness. On the other hand, the prognosis in schizophrenia and epilepsy is unfavorable, and in hebephrenia associated with weakmindedness very grave.

Zappert[379] reports seven cases of infantile dementia, an affection to which Heller first called attention in 1908. The symptoms appear in the third or fourth year of life, with disturbances of speech, which later becomes much aggravated until spontaneous speech and understanding of the heard word ceases. There exist restlessness, hallucinations, states of fear and dementia, that within a few months ends in complete idiocy, the condition finally becoming stationary.

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375. Comby, J.: Arch. de méd. d. enf. **24**:303 (May) 1921.
376. Gordon, H.: Brain **43**:313 (Jan.) 1921.
377. Strecker, E. A.: New York M. J. **114**:209 (Aug. 17) 1921.
378. Schnabel, J.: Ztschr. f. d. ges. Neurol. u. Psychiat. **68**:241, 1921.
379. Zappert: Monatschr. f. Kinderh. **22**:389, 1921.

The studies of the therapeutic effects of tuberculin and typhoid vaccine and especially of artificially inoculated malaria tertiana in progressive paralysis (dementia paralytica), as they have been carried out at the psychiatric clinic at Vienna for the last few years, are of considerable interest. Following the communication by Wagner-Jauregg[380] on this subject, Gerstmann[381] in his last report, gives a brief review of the results in thirty-nine patients treated from 1917 to May, 1920, with the plasmodium. Since September, 1919, 200 patients, most of them having dementia paralytica, and recently also patients having locomotor ataxia or tertiary and congenital syphilis were inoculated with tertiane plasmodium. After from nine to twelve malarial attacks, quinin-neoarsphenamin treatment is instituted. Among 116 cases studied thoroughly, thirty-eight cases, far advanced and of long standing, remained unimproved. Forty-two instances manifested complete remissions without any residual signs of psychic defect and thirty-six patients incomplete remissions with some residual symptoms. Extremely interesting observations were made, such as sudden alteration of the psychotic picture following the malaria attacks, and acute reactive intensification of the paralytic symptom complex until the remission took place after the antimalarial treatment. Encouraging results are reported also by Weygandt.[382]

MONGOLIAN IDIOCY

That mongolian imbeciles are often the last children of large families and physically exhausted mothers is reiterated by Comby.[383] He recalls the fact that they are more frequent among nations with a high than those with a low birth rate, such as the French. The first two claims are borne out also by the experiences of von Hofe.[384]

On the other hand, H. Thursfield[385] in his study of forty-two mongolians, finds no corroboration of the current statement that the mongoloid is apt to be the last child of a long family. He notes, however, that in six instances previous to the birth of the idiot the mothers had failed to bear children for a long period.

Stolzner's view of an existing causal connection between hypothyroidism of the mothers during pregnancy and mongolism is not borne out by Dollinger[386] who, on the contrary, in nineteen mothers, could establish anamnestically a slight hyperthyroidism. The author notes the

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380. Wagner-Jauregg: Wien. klin. Wchnschr. **34:**171 (April 14) 1921
381. Gerstmann, J.: Ztschr. f. ges. Neurol. u. Psychiat. **74:**242, 1922.
382. Weygandt: Deutsch. med. Wchnschr., 1921, p. 1013.
383. Comby, J.: Medicine **2:**835 (Aug.) 1921.
384. Von Hofe, F. H.: Arch. Pediat. **39:**737 (Nov.) 1922.
385. Thursfield, H.: Brit. J. Dis. Child. **18:**18 (Jan.-March) 1921.
386. Dollinger, A.: Ztschr. f. Kinderh. **27:**332 (Jan.) 1921.

increasing frequency of this anomaly and calls to mind that the theory of exhaustion by advanced age should be extended to the fathers.

An argument against a causative relationship between myxedema and mongolism is the fact brought out by Nadolny and Weinberg[387] that the blood picture in the latter shows no deviation from the normal and no similarity with the findings in myxedema; and that the basal metabolism, studied by Fleming[388] in six mongoloids, was normal and not affected by thyroid treatment.

Peculiar changes in the anterior portion of the fossa pituitaria consisting in an excavation under the anterior clinoid processes and optic groove have been described by Timme.[389] This condition in conjunction with certain clinical signs suggest to him a disturbance of the anterior part of the pituitary body as the cause of many of the symptoms of mongolism.

Mongolian idiocy in one of twins, a rare occurrence, has been reported by McLean[390] and Clay.[391] Clay invites investigation on the part of the obstetrician, as the determination of the monozygotic or dizygotic origin of such twins may aid in determining whether the cause of mongolian imbecility, occurring in one of twins, has a maternal or paternal etiology. Halbertsma[392] in connection with five new cases and nine from the literature on mongolianism in one of twins, advances the hypothesis that the underlying factor is malformation of the median part of the skull, a "vitium primae formationis" due to an endogenic element. The fact that among double-ovum twins the one is entirely normal seemed to point to an endogenous factor and the usually advanced age of the mother to the anomaly having its origin in the ovum. The occurrence of mongolian imbecility in the Mongolian race (Chinese) has been confirmed by a case report of Demuth[393] and Tumpeer.[394]

The anatomic pathology in a baby of 21 months described by Cozzolino[395] was the following: underweight brain, asymmetry of hemispheres, reduction of the thickness of cortex and of the number and extent of convolutions; marked underdevelopment of the lower frontal convolutions and an extension of the parieto-occipital fissure.

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387. Nadolny, G., and Weinberg, M.: Ztschr. f. Kinderh. **29**:68 (April) 1921.

388. Fleming, G. B.: Quart. J. Med. **16**:11 (Oct.) 1922.

389. Timme, W.: Mongolian Idiot; a Preliminary Note on Sella Turcica Findings, Arch. Neurol. & Psychiat. **5**:568 (May) 1921.

390. McLean, S.: Mongolian Idiocy in One of Twins, J. A. M. A. **78**:13 (Jan.) 1922.

391. Clay, H. T.: Arch. Pediat. **39**:726 (Nov.) 1922.

392. Halbertsma, T.: Nederlandsch Tijdschr. v. Geneesk. **2**:22, 1922; Zentralbl. f. ges. Kinderh. **13**:465, 1922 (abstr.).

393. Demuth, F.: Ztschr. f. Kinderh. **33**:110 (July) 1922.

394. Tumpeer, T. H.: Mongolian Idiocy, J. A. M. A. **79**:14 (July 1) 1922.

395. Cozzolino: Pediatria **29**:49 (Jan. 15) 1921.

CEREBROSPINAL FLUID

The fact that Dandy produced unilateral internal hydrocephalus by obstructing one foramen of Monroe and that extirpation of the choroid plexus in such an obstructed lateral ventricle prevented the development of internal hydrocephalus is declared by Weed [396] to be the strongest single piece of evidence that the origin of the cerebrospinal fluid is in the plexuses. However, there exists anatomic evidence that the perivascular spaces, the ependymal lining of the ventricles and the central canal of the spinal cord contribute a minimum addition to the fluid.

The constant amount of calcium in the liquor under physiologic and pathologic conditions, as found by Leicher [397] seem to indicate that the fluid is a secretion.

Xanthochromia has been reported in about 310 cases in the literature in connection with hemorrhages in the central nervous system and its membranes, hemorrhagic inflammation and pressure on the cord, whenever erythrocytes had found their way into the spinal fluid. The color, as demonstrated by Leschke [398] is due to bilirubin, formed from hemoglobin.

The presence of hemolysins in lumbar puncture fluid has been found by Schleissner [399] to be a reliable index for the presence of purulent meningitis and for the trend of recovery or aggravation. He recommends the greater use of Weil-Kafka's method by the pediatricians.

For the not infrequent cases in which only small quantities of cerebrospinal fluid are available, special micromethods have been worked out for cell count and various reactions. Detailed directions for various micromethods with a material varying from 1 to 15 drops are given by Plaut.[400]

A simple methylene-blue method for the qualitative and quantitative determination of the reducing substance in the cerebrospinal fluid is described by Michio Kasahara, and Shunjiro Hattori.[401] It is rapid, convenient and sufficiently accurate for practical use and is recommended also by Strong [402] for the less elaborately equipped laboratory.

In order to facilitate differentiation in the counting of lymphocytes from erythrocytes admixed in the spinal fluid, Jacobsthal [403] recom-

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396. Weed, L. H.: Psysiol. Rev. **2**:171 (April) 1922.

397. Leicher, H.: Deutsch. Arch. f. Klin. Med. **141**:196, 1922.

398. Leschke, E.: Deutsch. med. Wchnschr. **47**:376 (April 7) 1921.

399. Schleissner, F.: Med. Klin. **17**:1206 (Oct. 2) 1921.

400. Plaut, F.: Ztschr. f. ges. Neurol. u. Psychiat. **65**:373, 1921.

401. Kasahara, Michio, and Hattori, Shunjiro: Rapid Clinical Method for Determination of Reducing Substance in Cerebrospinal Fluid; Methylene Blue Method, Am. J. Dis. Child. **22**:218 (Aug.) 1921.

402. Strong, R. A.: Arch. Pediat. **39**:431 (July) 1922.

403. Jacobsthal, E.: Deutsch. med. Wchnschr. **48**:867 (June 30) 1922.

mends an increase in the concentration of the methylene-violet and the acetic acid according to his formula, which is given. The interferometer method of Loewe for determining the concentration of the cerebrospinal fluid as a diagnostic means in affections of the central nervous system is approved by Wüllenweber.[404]

The value of the routine use of the colloidal gold reaction in acute poliomyelitis becomes evident from the study of Regan and Cheney.[405] In every case during the acute stage there was a reaction in the "syphilitic zone," with typical rising and falling curves for the first and second weeks, thereafter gradually subsiding. The reaction may be of some use in the differential diagnosis of epidemic encephalitis. In conjunction with the clinical findings, the test may be the most valuable laboratory method we possess for the recognition of poliomyelitis. The authors believe that when the curve becomes normal, the acute period is over, and the more energetic treatment of the subacute stage may begin.

Of practical importance are the findings of Baar [406] that the globulin content may be increased in uremic-eclamptic attacks, and equal that in tuberculous meningitis, especially in repeated spasmophilic convulsions and in a number of organic affections of the central nervous system. A negative Pandy's reaction, excluding an increase of globulin, argues against tuberculosis in the differential diagnosis from clinically similar functional disorders. For the differential diagnosis between tuberculosis and other organic affections of the central nervous system with a similar symptom complex, the positive reaction is of little value, except that a continuous increase of its intensity would indicate tuberculosis. Aschenheim,[407] referring to the paper on Pandy's reaction by Widmaier,[408] cautions against an overvaluation of a positive Pandy's reaction for the diagnosis of tuberculous meningitis.

On account of the frequency of cerebrospinal involvement in prenatal syphilis, Kingery [409] stresses the importance of routine lumbar punctures.

The studies of comparative results of colloidal mastic and colloidal gold tests carried out by Keidel and Moore [410] with spinal fluid of 311 mostly syphilitic patients, warrant a wider use of the former than is now made, since it seems to detect anomalies more frequently than does the gold test. The liquor findings in congenital syphilis were studied by Tezner [411] with sixty-two punctures in forty-three children. In 41 per cent. the findings were positive. The Wassermann reaction was positive in 32 per cent. Pandy's test showed parallelism with Nonne's; other reactions lacked parallelism. The findings are evanescent and do not indicate a permanent injury to the central nervous system.

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[404] Wüllenweber, G.: München. med. Wchnschr. **69**:927 (June 23) 1922.

[405] Regan, J. C., and Cheney, G. W. H.: Value of Use of Colloidal Gold Reaction in Acute Epidemic Poliomyelitis, Am. J. Dis. Child. **23**:107 (Feb.) 1922.

[406] Baar, H.: Wien. klin. Wchnschr. **34**:614, 1921.

[407] Aschenheim, E.: München. med. Wchnschr. **68**:1015 (Aug. 12) 1921.

[408] Widmaier, E.: München. med. Wchnschr. **68**:772 (June 24) 1921.

[409] Kingery, L. B.: Study of Spinal Fluid in Congenital Syphilis, J. A. M. A. **76**:12 (Jan. 1) 1921.

[410] Keidel, A., and Moore, J. E.: Comparative Result of Colloidal Mastic and Colloidal Gold Tests, Arch. Neurol. & Psychiat. **6**:163 (Aug.) 1921.

Not only an excessive quantity of cerebrospinal fluid, with its increased intracranial pressure, but also hypotension associated with too little cerebrospinal fluid is liable to cause symptoms, as headache, vertigo, convulsions and torpor. Leriche [412] describes a few illustrative cases demonstrating this, and the beneficial effect of return to normal cerebrospinal pressure by cutaneous saline infusions. Similar symptoms occasionally followed lumbar puncture. Convulsions in children should, therefore, be studied with these considerations in view.

That lumbar puncture may involve serious dangers is emphasized by Guillain and Laroche,[413] especially in Pott's disease. They quote Sicard, who avoids puncture in bulbar affections.

Caronia and Auricchio [414] found the specific bacillus in typhoid and paratyphoid so regularly in the cerebrospinal fluid that they see in the examination a valuable diagnostic method in suspected typhoid.

REFLEXES

The statement generally made that changes in the classic deep reflexes have little diagnostic value in early infancy is borne out in the study by Burr [415] of sixty-nine normal infants. Among the reflexes, the plantar was the most variable, and the Achilles tendon reflex the most frequently lacking. Feldman [416] failed to obtain a plantar response in only 15 per cent. of 500 children from birth up to 7 years of age. While all observers, except Finizio, find the prevailing response of Babinski type in the very young, he found the proportions between plantar flexion and dorsiflexion to be 4 : 1. In premature infants, the response is nearly always of the Babinski type for from five to six weeks of postnatal life, because of the absence of myelinization of the pyramidal tracts. The definite disappearance of Babinski's type depends in his experience by no means on the age at which the child begins to walk.

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[411] Tezner, O.: Monatschr. f. Kinderh. **22**:4, 1921.

[412] Leriche, R.: Lyon. chir. **19**:57 (Jan.-Feb.) 1922.

[413] Guillain, G., and Laroche, G.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:794 (May 27) 1921.

[414] Caronia, G., and Auricchio, L.: Pediatria **30**:337 (April 15) 1922.

[415] Burr, C. W.: Reflexes in Early Infancy, Am. J. Dis. Child. **21**:529 (June) 1921.

[416] Feldman, W. M.: Brit. J. Child. Dis. **18**:24 (Jan.-March) 1921.

The contradictory reports on the oculocardiac reflex (Dagnini-Aschner) induced Sante Naccarati [417] to study it in normal and pathologic subjects. Some of his conclusions are that the reflex cannot constitute a positive sign for differential diagnosis, and that it may serve only as an indicator of probability. Large deviations from the reflex index may under certain conditions indicate abnormal states. In tabes, for instance, the reflex index is 0 or very small.

Resek [418] succeeded in provoking for the first time a conditional reflex (Babinski's). All laws of a conditional reflex pertaining to alterations of the stimulation inhibition and extinction were proved to exist.

Children of early school age, when asked to open the mouth wide for inspection, frequently exhibit peculiar associated movements to which Goett [419] calls attention. They consist in a stiffening of the body, marked abduction (spreading) of the fingers, with the arms stretched downward and the eyes opened wide. The movements are related to expressive movements and are induced by the subconscious idea of "opening" (mouth, eyes, fingers).

MISCELLANEOUS

Venipuncture of the superior longitudinal sinus appears to be the best method for obtaining blood from the new-born or for intravenous medication in infants. Gordon,[420] in 231 punctures, experienced no untoward results. At the Rostock children's clinic, it has been performed 3,000 times, as Krasemann [421] reports. For facilitating the procedure, Ratner [422] devised a new apparatus.

Wentzler [423] constructed a tonometer which, applied over the anterior fontanel, serves for the measurement of the intracranial pressure.

In a statistical survey of 100 cases of skull fractures in children, Moorhead and Weller [424] established a mortality of 17 per cent., associated injuries excluded. The mortality with involvement of the base was four times that of vault injuries alone. More than three fourths of the fatalities occurred in the first two days. In comparison with adults, children have a 25 per cent. better chance for life with the same grade of skull injury.

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[417] Naccarati, Sante: Oculocardiac Reflex (Dagnini-Aschner phenomenon) Its Use in Medicine and Psychology, Arch. Neurol. & Psychiat. **5**:40 (Jan.) 1921.

[418] Resek, F.: Ztschr. f. Kinderh. **29**:85 (April) 1921.

[419] Goett, T.: Ztschr. f. ges. Neurol. u. Psychiat. **66**:93, 1921.

[420] Gordon, J. W.: Venipuncture of Superior Longitudinal Sinus in New-Born; Results in 231 Cases, J. A. M. A. **77**:1721 (Nov. 26) 1921.

[421] Krasemann, E.: Med. Klin. **17**:809 (July 3) 1921.

[422] Ratner, A. B.: New Apparatus and Method for Puncturing the Superior Longitudinal Sinus, Am. J. Dis. Child. **21**:199 (Feb.) 1921.

[423] Wentzler, E.: Arch. f. Kinderh. **70**:241 (Jan.) 1922.

[424] Moorhead, J. J., and Weller, W.: Ann. Surg. **74**:72 (July) 1921.

The peculiarities of the chemical composition of the infantile brain were studied by Schiff and Stransky [425] in twelve cases. It was found that the water content diminishes with age, and that the dry substance of the infantile brain contains more albuminous substances and less lipoids than that of the adult. The cholesterin in infants is more than double that in the adult, and the unsaturated phosphatids are less than in the adult. On account of the large amount of proteins that are capable of inhibition and the scarcity of lipoids that inhibit it, the infantile brain is in a condition very favorable for inhibition, to which possibly the predisposition to convulsions at this age may have a relationship.

Cephalic bruit in infants and children was the subject of study by Still.[426] No connection with any particular disease could be established. The phenomenon is possibly due to the temporary tortuosity of the carotids at the base of the skull, and the occasional persistence of audibility beyond the usual age may be related to an unusual thinness of the bony wall of the carotid canal.

Paralysis in a number of children due to the bite of wood-tick (*Dermacentor venustus*) has been reported by McCornack.[427] The condition may issue fatally from respiratory failure if the large, engorged wood-tick, found mostly in the scalp, is not removed entirely. Otherwise, recovery is rapid.

An outbreak of botulism affecting eight persons and ending fatally in six has been reported by Whiteman and Wilkinson.[428] Two children were among the victims. They showed decided weakness of the arms, legs and neck, slight ptosis and dysphagia. Recovery was slow. Colver,[429] who saw five cases of botulism, two terminating fatally, recalls that the affection is a toxic encephalitis localized in the various nuclei of the pons and in the medulla, probably also in the thalamus opticus, and that clinically it may be confounded with epidemic encephalitis, methyl alcohol poisoning, poliomyelitis and meningitis.

An elaborate monograph on tachymeningitis hæmorrhagica interna in childhood with numerous illustrations and twenty-two case histories has been published by Rosenberg.[430]

Total hemihypertrophy of the body with mental defect, one of the rarest developmental anomalies, has been reported by Gesell [431] in a

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425. Schiff, E., and Stransky, E.: Jahrb. f. Kinderh. **96**:245, 1921.

426. Still, G. F.: Brit. J. Child. Dis. **18**:173 (Oct.-Dec.) 1921.

427. McCornack, P. D.: Paralysis in Children Due to Bite of Wood-Ticks, J. A. M. A. **77**:260 (July 23) 1921.

428. Whiteman, R. T., and Wilkinson, E. A.: Outbreak of Botulism, J. A. M. A. **78**:1278 (April 29) 1922.

429. Colver, B. N.: J. Michigan M. Soc. **20**:385 (Oct.) 1921.

430. Rosenberg, O.: Ergebn. d. inn. Med. u. Kinderh. **20**:549-638, 1921.

431. Gesell, A.: Hemihypertrophy and Mental Defect, Arch. Neurol. & Psych. **6**:400 (Oct.) 1921.

boy. A comprehensive tabulation shows a total of forty cases recorded in the medical literature, in five of which the patients were mentally defective. In Noronha's [432] case, the right side of the face was the larger and the trunk and limbs were larger on the left.

Posey [433] reports three cases of myasthenia gravis and Schäffer, with Brieger,[434] studied muscle tests in this affection.

Recklinghausen's disease has been reported by Parker [435] and Levin.[436]

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432. Noronha, A. J.: Indian M. Gaz., Calcutta **56**:10 (Jan.) 1921.

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ACUTE HEMORRHAGIC PANCREATITIS RESULTING FROM ROUNDWORMS

REPORT OF CASE *

W. E. GALLIE, M.D.
AND
ALAN BROWN, M.D.
TORONTO

Acute hemorrhagic pancreatitis in childhood is a rare disease. The case which is here reported is the only one that has been known to occur in the medical and surgical practice of the Hospital for Sick Children in a period of forty years. The reason for this rarity is evident when one considers that the conditions to which pancreatitis is usually attributed, such as gallstones and cholecystitis, are diseases of adult life.

The manner in which these conditions give rise to pancreatitis, or more specifically, cause trypsinogen of the pancreas to be converted into trypsin before it reaches the intestinal canal has been the subject of much investigation. It seems probable that the release of trypsin in the pancreas may be brought about by the introduction of either bacterial infection, through the lymphatics, blood stream or the pancreatic ducts, or of bile or duodenal juices, as the result of abnormal conditions at the ampulla of Vater. It has been demonstrated by Archibald and others that the injection of normal bile or intestinal juices into the pancreatic ducts will set up violent hemorrhagic pancreatitis, and cases have been recorded in which abnormalities at the ampulla, such as impacted gallstones, readily explain how it would be possible for a backwash of bile into the pancreas to occur. Two cases of severe pancreatitis have been described in which roundworms entered the ampulla and worked their way into the pancreatic duct. In one of the cases, described by Sir Hugh M. Rigby,[1] the condition was found at necropsy, and in the other, the patient was operated on by Novis,[2] and the roundworm removed. The successful result in the latter case appeals to us as a fitting reward for a masterly piece of surgery.

The case we have to record is another instance of pancreatitis produced, in all probability, by invasion of the ampulla by a roundworm.

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* Received for publication, Nov. 7, 1923.

* Read at the first annual meeting of the Canadian Society for the Study of Diseases of Children, Montreal, June, 1923.

[1] Rigby, H. M.: Brit. J. Surg. **10**:419 (Jan.) 1923.

[2] Novis: Brit. J. Surg. **10**:421 (Jan.) 1923.

The case is unique in that it occurred in a younger patient than any hitherto mentioned in the literature.

REPORT OF CASE

History.—A boy, aged 2½ years, thirty-six hours previously, at 6 a. m., began to cry with severe pain in the abdomen, doubling over and turning pale. He vomited in a few minutes and continued to vomit frequently until 3 p. m., when the pain, which had been continuous up to this time, ceased. The child was seen by Dr. Hewitt of Dunnville at 7 a. m., an hour after the onset of the symptoms, and a diagnosis of acute indigestion was made. He was seen again in the afternoon, and was given two simple enemas and later a milk and molasses enema, which were not effectual. A diagnosis of acute intestinal obstruction was made, and the patient was sent to Toronto. There was no history of intestinal worms and no report of previous illness except a mild attack of influenza about one week before.

Physical Examination.—The child was crying. The upper right side of the abdomen and the epigastrium were moderately rigid and apparently very tender. Crying was continuous, so that a satisfactory abdominal examination was impossible. There was no sign of shock. The child sat up in bed and cried lustily and fought against examination. Rectal examination was negative except that considerable gas of a fecal odor was passed. Under anesthesia, the abdomen was seen to be moderately distended. Running transversely across the abdomen, just below the level of the pylorus, a distinct tumor could be felt, firmly fixed in the posterior abdominal wall, about the thickness of one's thumb and about 3½ inches (8.7 cm.) long. No abnormality was noted elsewhere. The white blood cells numbered 15,000; polymorphonuclears, 68 per cent. Diagnosis: Partial intestinal obstruction with peritonitis from some unknown cause was diagnosed. The tumor was suggestive of intussusception, but it was too thin and too fixed, and the idea was abandoned before operation.

Operation.—At midnight, Feb. 15, 1923, forty hours after the onset of symptoms, the abdomen was opened by a right rectus incision. A small amount of blood stained fluid escaped, and considerable more was found among the coils of intestine. The transverse colon and great omentum were decidedly inflamed, and on the latter were observed numerous spots of fat necrosis about the size of a grain of wheat. Routine abdominal examination showed the appendix, cecum, small intestine and sigmoid colon normal. The gallbladder was distended, but showed no evidence of disease; it was easily emptied and contained no stones. The bile ducts seemed normal. The liver and stomach were normal. The tumor was then explored, and was found to be the pancreas covered with a mass of acutely inflamed swollen omentum. The mass was hemorrhagic and studded with dozens of patches of fat necrosis about the size of grains of wheat. All the peritoneum in the region of the pancreas and transverse colon, and also the great omentum and the neighboring small intestines were reddened and slightly sticky.

The blood stained fluid was mopped out of the peritoneal cavity. Drainage of the gallbladder was decided against. The abdomen was closed.

Course.—Following operation, the child slept quietly. There was no further pain or vomiting. During the day, the bowels were moved with an enema. At 3 p. m., i. e., fifteen hours after the operation, the patient was noticed to be gagging, and the nurse extracted a full sized roundworm from his mouth. Recovery was uneventful, and the child left the hospital at the end of ten days perfectly well.

COMMENT

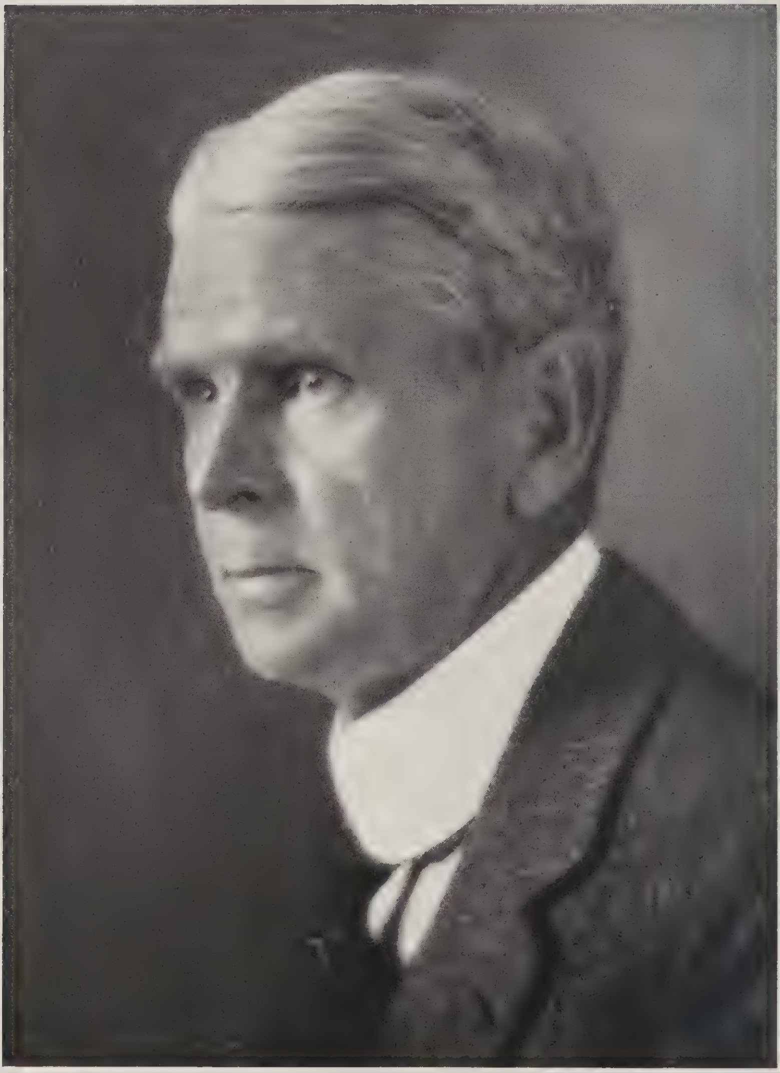
We are of the opinion that the symptoms were produced by the roundworm, which had either introduced its head into the ampulla of

Vater, thus allowing a back flow of bile or intestinal juices into the pancreas, or had created such an irritation in the duodenum that the ampulla became closed off by the resulting inflammatory reaction. The symptoms of abdominal pain, shock, vomiting and obstruction resulted from the pancreatitis and peritonitis so produced. We believe that the disappearance of the pain and vomiting at 3 p. m. on the day of the onset of symptoms indicated that the cause of the pancreatitis ceased to be active at that time, and at this moment the roundworm ceased to obstruct the ampulla.

We were surprised to learn that further treatment for roundworms failed to demonstrate any more worms.

DR. LUTHER EMMETT HOLT

Dr. L. Emmett Holt, since its foundation a member of the editorial board of the American Journal of the Diseases of Children, died, January 14, in Peking, China, where he had gone to deliver a course of lectures at the Union Medical College. An obituary notice will appear in the March issue.



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L. Emmett Holt.

OBITUARY

LUTHER EMMETT HOLT, M.D.

Dr. Luther Emmett Holt died of myocarditis on Jan. 14, 1924, in Pekin, China, where he had gone to give a course of lectures in the Pekin Union Medical College. Thus passed away the dominant figure in American Pediatrics.

Dr. Holt was born in Webster, New York, on March 4, 1855, the youngest son of Horace and Sabrah Curtice Holt. He received his undergraduate education at the University of Rochester, and after graduation in 1875, taught for a year at the Riverside Institute in Wellsville, New York. He studied at the Buffalo Medical College but received his degree from the College of Physicians and Surgeons (Columbia University) in 1880, and was appointed to an internship in Bellevue Hospital.

It was the fortunate and sympathetic association with Dr. Virgil P. Gibney during his medical school period that drew Dr. Holt toward the problems of disease in children, and thus directed the activities of the rest of his life. He served for many months as a student assistant in the Hospital for Ruptured and Crippled where Dr. Gibney was the chief surgeon, assisting in the endless duties of an active hospital. So much was he influenced by the interests thus formed that, as soon as he left Bellevue Hospital, he entered eagerly on the task of acquiring a broad knowledge of the diseases of infancy and childhood, then no easy task. Hospitals for children were usually designed primarily for orthopedic and surgical diseases, and in those where there were medical services these were discontinuous and insufficiently provided with assistants and facilities. It was, therefore, necessary for one who would be continuously at work, and such was always Dr. Holt's habit, to be connected with a number of institutions whose services would dovetail. So it was that he was on the staff of the following institutions, each for a number of years: The Northwestern Dispensary, the New York Infant Asylum, the New York Foundling Hospital and the Nursery and Child's Hospital. It was in the Babies' Hospital, however, with which he was intimately associated from 1889 until his death, that his chief clinical work was done. For many years he was the physician-in-chief. The growth of this institution was the result of his guiding hand. The Babies' Hospital began by occupying a dwelling house on Lexington Avenue. It grew to a large modern building with excellent equipment, while the medical studies that emanated from it gave to the hospital a world wide reputation.

Dr. Holt's contributions to medicine began early and continued uninterruptedly until his death. They embraced many aspects of pediatrics and were founded on a thorough pathologic knowledge. The most important related to the diseases of infancy and early childhood, which was always the field of his chief interest and occupation.

It was as a teacher that Dr. Holt was preeminent. He instructed undergraduates, and by his books and writings he taught the whole medical profession of this country. He was professor of diseases of children at the New York Polyclinic Hospital from 1890 to 1901, when he resigned to become Carpentier Professor of Diseases of Children at the College of Physicians and Surgeons (Columbia University) in succession to Abraham Jacobi. This professorship he held for twenty years. His success as a teacher depended on many things, an earnest desire to impart knowledge, an infinite capacity for taking pains, a clarity of thought that made complicated questions appear plain and a simplicity of exposition that could hardly be equaled. The same qualities appeared in his writings. Small wonder then, that the ears of his listeners and the eyes of his readers were many.

That Dr. Holt possessed the ability to think clearly and advise wisely was widely recognized. As a result, he was called on to play a major part in the development of important projects. He was one of the original board of directors of the Rockefeller Institute and was its secretary until his death. He gave much time and thought to the New York Academy of Medicine, and he was an editor of the AMERICAN JOURNAL OF DISEASES OF CHILDREN for more than ten years. Twice he was president of the American Pediatric Society. On resigning his chair at the College of Physicians and Surgeons he devoted an increasing amount of energy and thought to the American Child Health Association, of which he was first vice president. Attempts to prevent disease and death among children had always appealed to him and, when it became possible for him, he threw himself with the enthusiasm of youth and the wisdom of age into what seemed to him a veritable crusade for the betterment of the health of the young.

Dr. Holt was a trustee of the University of Rochester, and the recipient of many honors from institutions and learned societies. The world recognizes his accomplishments and regrets the loss of one who unselfishly has done so much for the public good. Those who knew him intimately have a keen, personal sorrow. He was to them a sincere, undemonstrative friend, revealing the warmth of his feeling by generous, unsolicited acts of kindness. One could not but recognize that he was honest and loyal to the core. There naturally followed admiration and affection. It was impossible to believe that there was anyone more worthy of trust. In the minds and hearts of many his memory will long remain.

John Howland.

American Journal of Diseases of Children

VOL. 27 MARCH, 1924 No. 3

ATONIC INSUFFICIENCY OF THE STOMACH A CAUSE OF VOMITING AND OF LACK OF APPETITE IN INFANTS *

GUSTAF LINDBERG, M.D.

NORRKÖPING, SWEDEN

Severe vomiting, endangering the development and even the life of the infant through the continuous loss of food, is most frequently met with in the new-born and during the first weeks of life. The cause of this vomiting may be a congenital stenosis or atresia of the intestinal canal, or more commonly a pylorospasm or a pyloric hypertrophy with stenosis. Less alarming cases of vomiting are also more frequently seen during the first period of life than later. While the causes already mentioned are fairly well recognized, the etiology of this milder type of vomiting remains rather obscure; and now and then one observes cases in which severe vomiting is due to none of the conditions mentioned. Some observations that seem to throw light on this particular point will be reported in this paper.

The type of vomiting I refer to is usually called habitual vomiting. Among the causes suggested, usually in a rather vague way, I mention aerophagy. The swallowed air is supposed to cause an explosive emptying of the stomach through the cardia. An abnormal sensitivity of the mucous membrane has also been considered a cause, particular emphasis being given to a neuropathic constitution. All of these cases, as is generally recognized, show no peristalsis of the stomach, and no pyloric tumor can be palpated.

I have observed several cases where another mechanism was responsible for the vomiting and here report a typical instance.

REPORT OF CASE

E. B., a full-term baby girl, with an initial weight of 3,400 gm., born of healthy parents, but a nervous mother, and who nursed energetically, started to vomit after two days. The vomiting, not very marked at the beginning, gradually became more frequent and voluminous. It occurred after the meal or after a short interval, and was for the most part not projectile. In spite of decreasing weight, the general condition remained rather satisfactory for some days. At the beginning of the second week, the weight dropped more rapidly, and there was loss of appetite. The baby vomited after every meal and frequently also a long time after the meal. The vomiting was now

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* Received for publication, Sept. 10, 1923.

* From the pediatric service of Norrköping City Hospital.

voluminous and projectile. The temperature was subnormal, and the baby was rather dull. The vomited material was often yellowish. The stools were soft, yellow and scanty.

I saw the baby for the first time two weeks after birth. The general condition was poor; the eyes were sunken, and the skin was inelastic and slightly icteroid. There was marked drowsiness. The heart and lungs showed no abnormal signs. The upper left quarter of the abdomen was slightly distended. Here a distinct peristalsis of the stomach was seen, with waves starting far to the left and progressing up to the midline, but not extending beyond. On percussion of the abdomen, vomiting readily occurred and the distension entirely disappeared. Owing to its serious condition, the baby was transferred to the

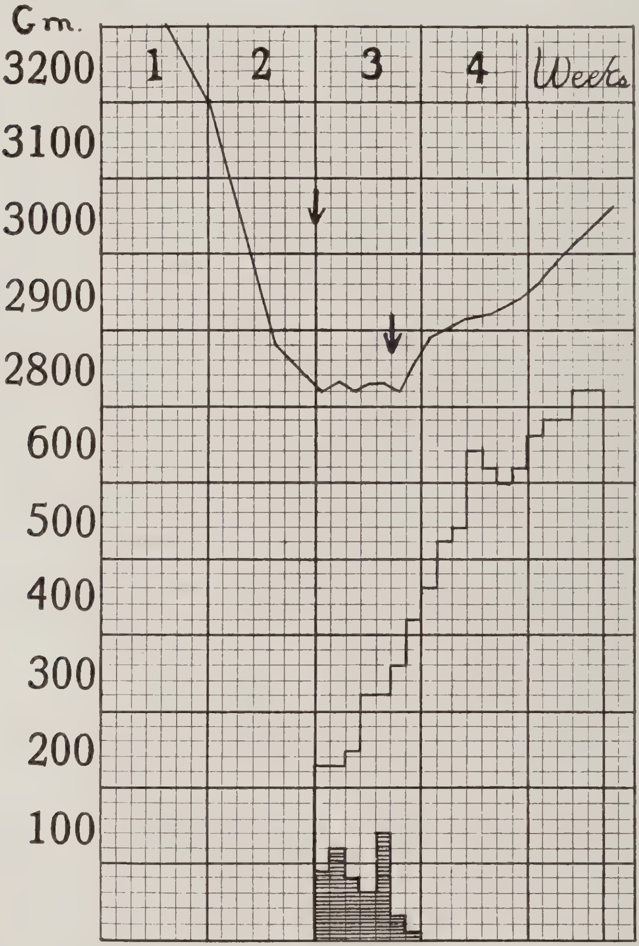

Fig. 1.—The upper curve represents the weight. The first arrow indicates the day when the hypodermic Ringer injections were started. The second arrow indicates when the Ringer injections were discontinued and the new therapy, with the baby in the vertical position, was introduced. The lower curve represents the amount of milk taken in twenty-four hours. The shaded area represents the amount of milk vomited in twenty-four hours.

hospital. Weight at admission was 2,800 gm. The general condition was unchanged. The baby was nursed eight times a day as it had been while at home. To prevent further drop in weight, a hypodermic injection of 100 c.c. of Ringer solution was given daily. Figure 1 charts the course in the hospital. The first arrow indicates the day of admission. The appetite was very poor, only 200 to 300 c.c. a day being taken in eight meals, at the age of 2 weeks, although there was a plentiful supply of breast milk. About half the milk taken was vomited, and the baby was in a severe state of starvation.

By the administration of Ringer's solution, it was possible to prevent further loss of weight, but at the same time it was evident that we had to do with a serious condition, and the prognosis was considered doubtful. The diagnosis of pylorospasm was of course considered, but against this diagnosis stood the fact that the vomited stomach content sometimes showed a discoloration due to bile. Trials with papaverin and atropin proved unsuccessful in this case, as in numerous others.

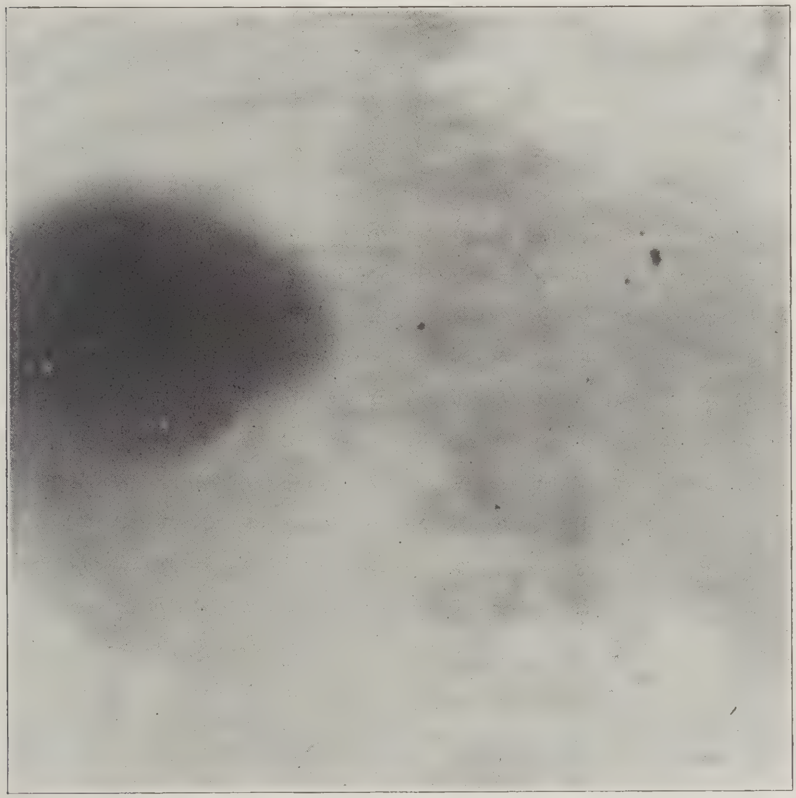

Fig. 2.—Roentgenograms taken with child in horizontal position, 100 gm. of breast-milk and 5 gm. of "contrast powder" having been introduced. The stomach does not empty.

To reach a definite diagnosis, the function of the stomach was studied under the fluoroscope, with an unexpected result. The examination was made in the morning, on an empty stomach. Through a fine catheter, 100 c.c. of breast milk mixed with 5 gm. of "contrast powder" was introduced into the stomach. This was done with the patient lying down, and the behavior of the stomach was observed every five minutes.

As shown in Figure 2, none of the stomach contents passed through the pylorus as long as the baby remained in the horizontal position. In correspondence with the distension visible on the abdominal wall, the stomach contents had accumulated to the left of the vertebral column. In spite of clearly visible peristalsis, nothing was passed on through the pylorus. Peristaltic waves occurred now and then, but there were no signs of a tonic contraction of the stomach around its contents. This condition of insufficiency lasted as long as the baby remained in this position.

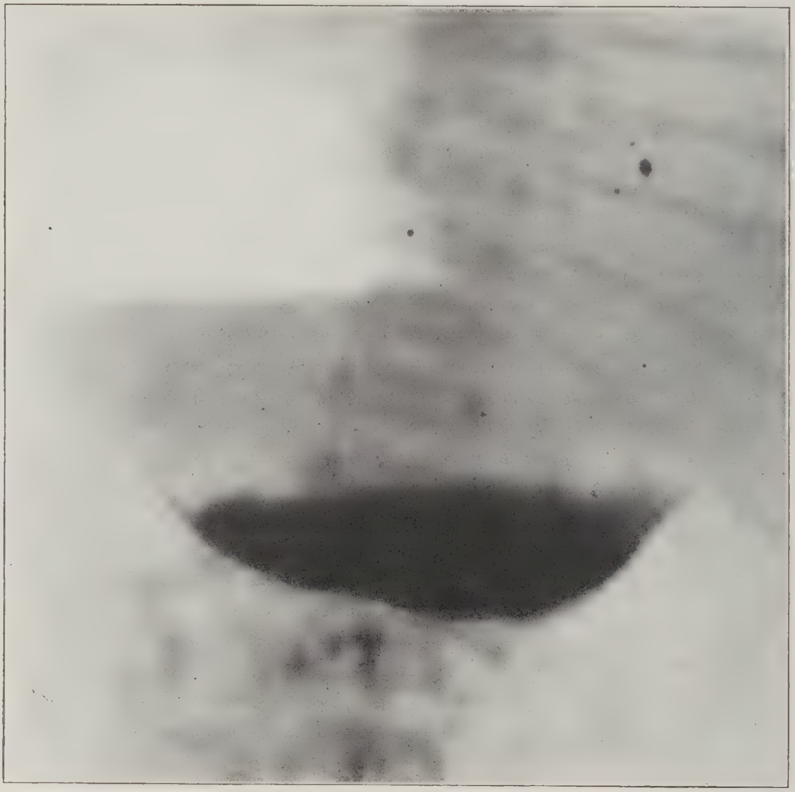

Fig. 3.—Roentgenogram taken with child in vertical position. The emptying of the stomach into the duodenum and the jejunum starts at once.

The observations were continued with the baby in the vertical position. The surprising fact was then immediately brought out that, as soon as the position was changed, the stomach contents at once started to pass over into the duodenum, and abundantly (Fig. 3). Even in this new position, there was a complete absence of tonic contraction, only a moderate peristalsis with big waves being seen. In the vertical position, the stomach now emptied rapidly, so that, after fifteen minutes, large amounts of the contrast meal were seen low down in the small intestine.

Since it had thus been proved by the roentgen-ray examination that no pyloric or other kind of obstruction prevented the emptying of the stomach, and it also was clear that the emptying took place in a vertical but not in a horizontal position, the baby was fixed almost upright in the bed by the aid of pillows and a strap around the chest and underneath the arms. The day for this change is designated in Figure 1 by the second arrow. The rest of the curve demonstrates the correctness of the conclusion drawn from the roentgen-ray examination. The vomiting completely disappeared at once, and a rapid growth in weight set in, in spite of the discontinuance of the Ringer injections. This improvement continued steadily, the appetite increased at once and no vomiting occurred unless the baby was lowered to a horizontal position. After three weeks, the baby could lie down without vomiting, and later development was normal.

To understand the pathogenesis of the clinical picture described, it is necessary to know the function of the stomach in the baby, as this function has been made known to us by earlier roentgen-ray studies. As Groedel first pointed out, the stomach in the adult possesses a double function. First, it has a tonic function, the walls of the stomach contracting around its contents, giving to the stomach a varying volume and shape according to the degree of fulness. Stiller called this the peristolic function, this name having been generally accepted. The second function is the peristalsis, consisting of waves of contraction progressing from the cardia toward the pylorus. The emptying of the stomach occurs through the joint peristolic and peristaltic action. The stomach of a normal infant differs from the stomach of an adult both in shape and in function, as was brought out by the first roentgen-ray studies on the subject. Thus, Leven and Barrett showed that the stomach of the infant does not contract around its contents, which means the peristolic function is not developed. This has been confirmed by later investigators, Flesch-Peteri,[1] Epstein [2] and others. The peristaltic function occurs as in adults and is, as a rule, sufficient for the satisfactory emptying of the stomach. Because of the absence of the peristolic function, the infant's stomach is like a flaccid balloon, changing shape and position according to the amount of its contents and the position of the baby. It remains completely distended, having only a small content, and a large "stomach bladder" is normal in the infant. Further, it was observed by Flesch-Peteri that the absence of a peristolic function depends on the nature of the content. If the milk is replaced by food of more solid consistency, a powerful tonic contraction around the content occurs even in the infant. There seems, therefore, no difficulty in arousing the peristolic function, through providing a sufficiently substantial stomach content. Epstein has confirmed this, and he has, like other investigators, both earlier and later, employed solid food in treating vomiting in infants.

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[1] Flesch-Peteri: Magenuntersuchungen mittels Roentgenstrahlen im Saeugelingsalter, Ztschr. f. Kinderh. **2,** 1911.

[2] Epstein, B.: Ueber die Beeinflussung des habituellen Erbrechens des Saeuglings durch Brei-Verfuetterung, Jahrb. f. Kinderh. **93:**360, 1920.

Correlating these facts with the observations in the case here reported, there seems to be no doubt that the inability of the stomach to empty itself in a normal way when the baby was in a horizontal position was due to the absence of a proper peristolic function. This is confirmed by a successful outcome of the therapy indicated by the roentgen-ray examination. When the conditions for the emptying of the stomach were improved by the vertical position, the vomiting ceased. Trials with solid food were unsuccessful in this case; in similar cases, I have, however, found solid food useful.

At first, I was inclined to look on the case just reported as a mere oddity. But having had my attention drawn in this direction, observation of other cases of loss of appetite or vomiting in the new-born or young infants during the first weeks of life gradually made it clear to me that the cause was not infrequently the same as in the case described. In cases of vomiting without signs of pylorospasm or any other obstacle to the emptying of the stomach, I repeatedly observed the same therapeutic result from the use of the vertical position described. Infants with a persistent lack of appetite preventing any gain in weight showed an immediate improvement or complete recovery after the simple change from the horizontal position to the vertical one. These observations refer, however, to the first weeks of life only. I do not know whether the same mechanism can be the cause of vomiting and lack of appetite in older infants. But I consider it improbable that this type of insufficiency here plays any independent rôle. At least, I have always found a normal motor function of the stomach as soon as the infants have passed the first months. During or after any nutritional disorder in older bottle-fed babies, the atony of the stomach is a factor of recognized importance.

It seems interesting to correlate with the findings here presented the common practice of mothers in handling babies when they vomit. The manner of carrying the baby in a half-erect position, slowly rocking it back and forth, continued for some time after each meal, seems now rational enough and is undoubtedly of therapeutic value. This therapeutic effect has been explained as due to a diminution of the amount of air present in the stomach, the air being more easily expelled through the cardia. It is easy to observe that this is often the case. In the case described here, however, the "stomach bladder" seemed bigger in the vertical position than in the horizontal. The main benefit of carrying the babies in a more or less vertical position is, therefore, in all probability, an easier emptying of the stomach.

The peristalsis observed through the abdominal wall in the case described deserves particular attention; and this is not only from a theoretical point of view. At present, it is generally accepted [3] that a visible peristalsis occurs only in pylorospasm or pylorostenosis of some other origin. In my case, this is easily ruled out. On the screen, the pylorus was wide open, and the vomited material had been observed sometimes to be colored by duodenal contents. Nevertheless, peristaltic waves were repeatedly observed through the abdominal wall, sometimes quite marked. This proves that visible peristaltic waves are not pathognomonic for pylorostenosis, as has generally been considered. Because of the content of air and fluid, the anterior wall of the atonic stomach in my case was evidently quite close to the thin abdominal wall. Peristaltic waves may thus become visible without being any stronger than normal. This brings up the question as to whether some of the mild cases of "pylorospasm," in which the symptoms disappear as soon as small and repeated meals are given and the stomach perhaps has been washed out twice, are correctly diagnosed as pylorospasm, or rather belong to the type of tonic insufficiency here described. The majority of the cases of pylorospasm are, of course, of a more serious type, but in some cases treatment consisting in merely a change in position may be tried.

Finally, I wish to emphasize again that not only vomiting but also lack of appetite in the new-born may be due to this atonic condition, and may be tentatively treated accordingly.

CONCLUSIONS

1. At birth and during the first weeks of life, incomplete emptying of the stomach is not an uncommon finding.
2. The symptoms are vomiting or lack of appetite, or both.
3. The symptoms may disappear if the baby is kept in a half-erect position.
4. These cases may simulate a pylorospasm.
5. Peristalsis visible through the abdominal wall may sometimes be observed without pylorospasm or pylorostenosis being present.

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[3] Finkelstein: Lehrbuch der Saeugelingskrankheiten, Ed. 2, Berlin, 1921.

GENITO-SUPRARENAL SYNDROME (SUPRARENAL VIRILISM) IN A GIRL ONE AND A HALF YEARS OLD, WITH SUCCESSFUL OPERATION *

ARTHUR COLLETT, M.D.

CHRISTIANIA, NORWAY

Hippocrates[1] described two cases of virilism in married women, whose bodies resembled the male's and were covered with hair. These women had a beard, and their voices were deep. Vesal describes similar cases. William Cooke (1756) was the first to give a more exact description of a case, in connection with a suprarenal gland tumor in a 7-year-old girl. She was enormously fat, with a thick growth of hair on the face and genital organs. Analogous observations have at times been made by many authors. Bevern and Romkild (1802) describe a 3½-year-old girl, who looked like a woman of 20, with a thick growth of hair on the genital organs and on the face.

Tilesius (1803) described a 4-year-old girl, enormously fat, with premature development of the breasts, and hair on the genital organs, and with a tumor the size of a goose egg in the left suprarenal gland. Bulloch and Sequeira[2] (1905) were the first to point out when describing a similar case in an 11-year-old girl, that the tumor develops in the suprarenal cortex. Bulloch and Sequeira further state that the other endocrine organs in the patient were normal, but they could not find the thymus. They have collected twelve cases of tumor of the suprarenal gland with sexual changes (inclusive of their own case) and thirteen cases without such changes, and with these cases as a basis give valuable assistance in making clear the connection between the tumors of the suprarenal glands and the sexual organs. Their conclusions will be mentioned later.

While Bullock and Sequeira, in their excellent treatment of the subject, restrict themselves to the condition of children. Bortz, in 1909,

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* Received for publication, Oct. 31, 1923.

* From children's section of the State Hospital.

* The case was presented before the Norwegian Medical Association in Christiania, Oct. 27, 1920 (referred in the publications of the Association, 1920, p. 116), and at the second Northern Pediatrics Congress in Stockholm, June, 1921 (Congr. forh., p. 134), under the title "Hermaphrodism and Too Early Sex-Development in a One and One-Half Year Old Child."

[1] The historical data are principally from Bulloch and Sequeira and Gallais, and from Biedl (Innere Secretion, 1916).

[2] Bulloch and Sequeira: On the Relation of the Suprarenal Capsules to the Sexual Organs, Path. Soc. of London, 1905.

described the disease in adults. Neugebauer (1908) had already determined that suprarenal glands were enlarged in a number of pseudo hermaphrodites (of female mold externally).

Apert[3] (1910) collected thirty-five cases, with necropsy, in persons of all ages (none of his own observation) and showed clearly that all the different descriptions represent different types of the same disease, the manifestations of which change according to the age at which the disease develops, but the nature of which is always the same. Like Bulloch and Sequeira, Apert maintains that there is a special syndrome arising from the changes in the suprarenal cortex. He gives the following forms: (1) hyperepinephry (with hyperplasia of the cortex), with (*a*) a marked growth of beard, (*b*) excessive growth of fat tissue and (*c*) early development of the body, with disturbances of the genital functions (thirty-one cases); (2) hypo-epinephry (with hypoplasia of the cortex), with (*a*) scant growth of hair, (*b*) poor development of fat tissue and (*c*) underdevelopment of the body (four cases).

According to Apert, there are distinguishable five types of hyperepinephry, varying according to the age of the individual at the time of the appearance of the disease, but all with the three above-mentioned symptoms. Most of these symptoms are seen in women.

1. *Hyperepinephry of the Embryonal Period.*—Hyperepinephry in this early period results in the individual becoming a hermaphrodite, with internal female genital organs, but outwardly of masculine form, with undeveloped breasts; hypospadiac clitoris peniformis; vulva like a cul de sac; uterus and ovaries. There is marked hypertrophy of the suprarenal glands.

2. *Hyperepinephry of Fetal Period.*—The anomaly is less pronounced, but there is no doubt as to the sex. There is a large clitoris, the uterus and ovaries are atrophied, and hypertrichosis is present. The hyperplasia of the suprarenal gland probably dates from the later period of fetal life.

3. *Hyperepinephry of the Prepuberty Period.*—There is (*a*) abnormal body development, with pubertas precox; (*b*) adipositas; (*c*) hypertrichosis, and (*d*) partial hypertrophy of the clitoris.

4. *Hyperepinephry of Maturity.*—Menstruation stops, and marked adipositas and hypertrichosis are present.

5. *Hyperepinephry During the Period Near and After the Menopause.*—The clinical picture here is indistinct. There is marked adipositas, and of disturbances of the genital functions metrorrhagia, and not even hypertrichosis is present.

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[3] Apert, E.: Dystrophies en relation avec des lésions de capsules surrénales, hirsutisme et progeria, Bull. Soc. de pédiat. de Paris **12**:501, 1910.

It is noticeable that the earlier the condition develops, the more marked are the changes.

Because the most constant symptom of hyperepinephry is hypertrichosis, Apert calls the disease hirsutism. The opposite condition is called by Gilford progeria (aged before time), and by Variot it is called "nanisme senile."

Alfred Gallais,[4] who has written a comprehensive treatise on the subject (1914), calls the clinical aspect produced by hypertrophy (physiologic or neoplastic) of the suprarenal gland "Le syndrome génito-surrénal."

This syndrome manifests itself, according to Gallais, in four forms: (1) le pseudo-hermaphrodisme surrénal (the disease occurs before birth); (2) le virilisme surrénal (the disease occurs after birth; the genital organs are formed); (3) la forme menstruelle; (4) la forme obstétricale.

The two last forms are characterized by E. Glynn[5] (1921) as superfluous and of doubtful justification.

If one reads the history of the disease, it is found that Gallais' cases are not always distinct. The first two forms correspond, as will be seen, to Apert's four forms.

Glynn prefers to classify all cases of abnormal sex character with tumor of the suprarenal gland under the name of suprarenal virilism. Since Apert's treatise, our knowledge of the symptoms and course of genitosuprarenal syndrome has been extended by a number of observations on individuals of all ages. Gallais, in 1914, refers to no less than fifty-one cases, among them four of his own observation. All of them were in women and children; reference is made to a doubtful case in a man. It thus appears that these tumors of the suprarenal gland do not cause sex changes in men.

At that time there were seventeen cases in children, collected by Glynn. Later one was observed by Tschernobrow[6] (in an 11-year-old boy); one by Schiff (in a 2-year-old girl), and one by Hijmans[7] (in a 3-year-old girl). These, with my case (in a 1½-year-old girl), total twenty-one cases, four of which were in boys.

There is no sex change seen in boys, but too early development, hypertrichosis and premature development of the outer genital organs, without potency. Sex power develops later, and slowly. In girls, menstruation does not appear early. Bulloch's and Sequeira's case, in which it occurred at 9 3/4 years, is an exception. As a rule in this syndrome, there is a false pubertas precox, as only the secondary sex characters are developed prematurely. Illustrating the real pubertas precox is Craterus' case: An individual was, in the course of seven years, a child, a youth, an adult, a father and dead.

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[4] Gallais, Alfred: Le syndrome génito-surrénal, Paris, 1914.

[5] Glynn, E.: A Comparison Between Ovarian "Hypernephroma" and Luteoma and Suprarenal Hypernephroma, with Comments on Suprarenal Virilisme, J. Obst. & Gynec. Brit. Emp., 1921, p. 48.

[6] Tschernobrow, E.: Ueber eine Geschwulst der Nebenniere bei einem 11 jährigen Knaben mit frühzeitger Geschlechtsentwicklung, Zürich, 1919.

[7] Hijmans, cited by Glynn, Footnote 5.

The marked development of the body may be manifested either as obesity or as great muscular development (l'enfant Hercule).

The hair growth in girls is most often of masculine type, but in the case of our patient the pubes were bounded horizontally, while the hair growth was otherwise even hypervirile. Ossification and dentition are often hastened. Thus, in the case of our patient, ossification corresponded to that of a 3-year-old child and the pelvis was of a masculine type. The development of the teeth was normal.

According to Leiner,[8] a child with the genitosuprarenal syndrome is dull and intellectually subnormal. On the contrary, our patient was lively and sensitive, with a mature expression. Hijman's 3-year-old girl was of similar type. In the most complete form of suprarenal virilism (with acquired lesion), Gallais claims that one can distinguish two phases in development. In the first phase, there is amenorrhea, sometimes accompanied by pains of the pelvis, nausea and vomiting. Adipositas, hyperasthenia, nervousness, strange mental phenomena are present and the sexual instinct deviates; the character is changed, and the patient becomes violent. There may appear crises of terror. Masculine hypertrichosis is constant; pigmentation, such as is shown in dirty gray spots on the forehead, in front of the armpits and on the back, forearms and the hand, is rare. In the second phase, there is emaciation, with red stripes on the abdomen, armpits, groins, etc.; progressive asthenia, and irradiating breast and loin pains. A tumor may be palpated in the abdomen. The patient may be without will power, and filled with suicidal thoughts.

ETIOLOGY AND PATHOGENESIS

The cause of tumor of the suprarenal gland is just as obscure as the cause of other tumors. As regards the suprarenal syndrome, Gallais states that in one case the patient's mother, in another case the patient's father, had died of tumor. Our patient's grandmother on the father's side had cancer of the breast. There are cases of nervousness in the family, as in our case, together with malformation from birth, as, for instance, hare-lip. As mentioned above, there has been no case reported in men; and in children, girls are far more frequently attacked than boys (17:4). With regard to localization of the tumors, it is agreed that tumors in the suprarenal *medulla* are never accompanied by changes in sex characteristics. These tumors are always situated in the cortex. They may arise partly from accessory suprarenal glands (these consist always of cortex substance) in the broad ligament (Bovin).

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[8] Leiner, J. H.: Pubertas Præcox with Especial Attention to Mentality, Endocrinology **4**:369 (July-Sept.) 1920.

Cases of the syndrome with hypernephroma in the ovary are described by Debeyre and Riche (Gallais, p. 221), but Bovin[9] (1909) and Glynn[5] (1921) both hold that there has not yet been produced certain proof of the existence of real hypernephroma in either the ovary or the testis, but quite near to them and then most often in children. Of hypernephromas in the kidney, Glynn and Hewetson[10] say that they are quite different in structure from those in the suprarenal gland and are never accompanied by sex disturbances. Gallais states that changes in sex characteristics are found only in adenomatous hypertrophy, adenoma or malignant hypernephroma, but not in sarcoma. However, in Bulloch and Sequeira's statistics are found two cases of virilism with large-cell sarcoma in the suprarenal gland (Colcote, Fox's and Ritchie's). Bulloch and Sequeira, however, say of Ritchie's cases that from microscopic examination, the histogenesis of the tumor is difficult to decide, though the type is sarcomatous.

It appears from the observations both of these authors and of others that in any case, sarcoma only exceptionally produces the syndrome. On the other hand, adenoma or tumor of the carcinomatous type does not always produce sex changes (Brüchanow's case in a 14-months-old girl; Rupprecht's case in a 2 ½-year-old girl may be cited).

With regard to the manner in which hyperplasia of the suprarenal cortex and tumor respectively produces the genitosuprarenal syndrome, there prevail various hypotheses. It is commonly supposed to be due to a hyperactivity of the supposed physiologic function of the cortex, which should promote the growth of the body and development of the secondary sex characteristics (Bulloch and Sequeira, Neurath,[11] Glynn,[5] Falta[12] and others). There is by some supposed to be a pluriglandular disturbance. Thus, for example, the hyperfunction of the cortex may secondarily influence the ovary (Wiesel, Gallais); while Blanchard,[13] supported by Pierre Marie[14] sees the cause exclusively in the disturbances in the sex gland. One more theory (Krabbe)[15] supposes that the appearance of the disease is due to the fact that the tumor develops from sex gland cells of masculine type, which early in the life of the embryo have been involved in the suprarenal gland cortex. The possibility of such a displacement of the sex gland cells has been pointed out by Bulloch and Sequeira. Krabbe's theory will again be referred to.

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[9] Bovin: Nord. med. Arch. **41**:4, Part 1, No. 15, 1908.

[10] Glynn, E., and Hewetson, J. T.: J. Pathol. & Bacteriol. **18**:81, 1913-1914.

[11] Neurath: Die vorzeitige Geschlechtsentwicklung, Ergebn. d. inn. Med., No. 4, 1909.

[12] Falta: Die Erkrankungen der Blutdrüsen, 1913.

[13] Blanchard, R.: Bull. de l'Acad. de méd., Paris **76**:47 (July 18) 1916.

[14] Pierre Marie, quoted by Blanchard, Footnote 13.

[15] Krabbe, K. H.: The Relation Between the Adrenal Cortex and Sexual Development, New York M. J. **114**:4 (July 6) 1921.

Both the proximity of the germ of the suprarenal cortex to the germ of the sex gland, and certain physiologic conditions, indicate a near relationship between the functions of these organs. The suprarenal gland cortex and the sex gland both arise in the celomicepithelium, where the germs are closely associated, without any sharp boundaries, even intermingling, in part (Brachet,[16] p. 556). The relation, according to Soulié, is at an earlier stage so intimate that it is impossible to distinguish the tissues from each other.

Meckel (1806) thought that a functional connection between the two organs could be noted, as he found extremely well developed sex organs and very large suprarenal glands in guinea-pigs, and Nagel found similar conditions. The latter proved that, in birds and amphibious creatures, the suprarenal glands are swollen during the rutting season. According to W. Kolmer, the structure of the suprarenal gland cortex varies in guinea-pigs according to sex, age and the condition of the genital organs, so that one can actually speak of a secondary sex character in the suprarenal gland. In the female of this species, according to the same author, there occur cyclic changes in the suprarenal gland parallel with the functions of the genital organs. There is supposed to have been observed a compensatory hypertrophy of the suprarenal gland, especially of the cortex after double castration (Théodossief, Ciaccio). The remaining aspects of the supposed functions of the suprarenal gland will not be further discussed here, but it should be noted that the whole physiology of the cortex is still *sub judice*.

Even Gallais made reservations as regards the physiologic function of the cortex because of the influence of the tumor on the sex character; while Krabbe disregards the theory of the tumor's influence as a cortex hypersecretion. "Why should such produce a masculine puberty in girls and not a feminine one?" This characteristic influence must, according to Krabbe, be explained in quite another way. He supposes, in support of his interesting theory, that while the testis is developed almost directly from the original undifferentiated germ of the sex glands, the ovary passes through a stage wherein its cortex is feminine, while the medullary is testicular; a consideration which is founded on investigations of Laulanié, among others, and confirmed by a number of authorities, among them A. Kohn and Brachet.[16]

It is precisely this medullary, testicular part of the ovary which, at an early stage, is closely connected with the suprarenal gland cortex and which, according to Krabbe, should be involved in the suprarenal gland cortex during further development. Hypernephroma in girls with virilism are supposed by him to be produced from these testicular cells. and that through secretion of the testicular hormones masculation is produced. In a similar way, the hypernephroma developing in boys from displaced testicular cells cause too early sex development. Krabbe's theory agrees well with Conheim's theory about the development of tumors from displaced cells. It may be of interest in this connection to quote (p. 558) the embryologist A. Brachet in regard to the functional connection between the suprarenal gland cortex and the sex glands: "Not only are physiologic relations proved, but, with due regard for what the future may show, one may even question whether the proliferations of the germinal epithelium and of the interrenal ridge are not in reality one and the same formation, the destiny of which is determined by the symbiosis established between it and elements derived from another source—a symbiosis with gonocytes on the one hand and chromaffin cells on the other." (Les connexions physiologiques ne sont nullement démontrés mais, toutes réserves faites sur ce que réserve l'avenir on peut se demander si les proliférations de l'épithélium germinatif et de la bandelette interrénale ne sont pas en réalité, une et même formation dont la destinée est déterminée par la nature de la symbiose qui s'établit entre elle et des éléments issus d'autre source: Symbiose avec gonocytes d'une part, avec les cellules phaéchromes de l'autre.)

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[16] 16. Brachet, A.: Traité d'Embryologie des Vertébrés, Paris, Masson & Cie, 1921.

During a tour in West Norway in the summer of 1920, I had an opportunity to examine a child of extraordinary appearance. With the cooperation of Prof. Axel Johannessen, I obtained permission to place the child in the state hospital, Christiania, children's ward, so that further investigations could be made.

REPORT OF CASE

History.—M. E. M., born March 18, 1919, admitted to the hospital Sept. 8, 1920, discharged Oct. 30, 1920, was of a healthy family. There was some nervous affliction on the father's side, and the paternal grandmother had cancer of the breast. Both father and mother were healthy and well built, of medium height, good appearance and very intelligent. The mother had a rather deep voice. There had been no abnormities, such as that of the patient, in the family. The patient was the youngest of five brothers and sisters, all healthy and normal. Pregnancy was normal. The mother, in the third month, fell over a 30-foot precipice, with a horse and cart. She escaped with a fright. The child weighed at birth 5,000 gm. (the weight of all the brothers and sisters at birth was about the same), and had grown steadily. She was breast fed for four or five months. Later, little by little, cow's milk, porridge, vegetables and fish were given her. She had been healthy except that in December, 1919, at 9 months of age, she developed whooping-cough. In February, 1920, she had severe bronchitis with convulsions. So far as the parents could remember, an abnormal growth of hair on the genital organs began before the whooping-cough, at from 6 to 8 months of age; but not until after the bronchitis had the growth of hair become thicker and extended over the trunk and extremities, just as the voice took on a deep rough sound, while before it was childish and clear. She gradually became heavy and fat, with bulging cheeks. She had been lively and not backward in mental development; on the contrary, the mother thought she was far quicker and cleverer than the other children were at a corresponding age. She could not yet walk or stand. The first teeth came at 5 or 6 months, as in the case of her brothers and sisters. It had been difficult to keep the skin free from roughness, and the cheeks had constantly been red and sore.

The parents had not noticed any abnormity in the form of the sexual organs. Bleeding from the genital organs had not been observed.

Examination.—The weight on admission was 15.10 kg. average (Camerer, 11.45 kg.; Holt, 10.68); the height, 80.75 cm. (Camerer, 79 cm.; Holt, 75.6); breast circumference, 53.5 cm. (Holt, 45.9); circumference of abdomen, 62.5 cm.; height, sitting, 50.5 cm.; head circumference, 49 cm. (Holt, 45.9). The child was heavily and plumply built, with a rather large head (Fig. 1). The face especially was bulging with fat; the cheeks were baggy. The ears were well-formed. The eyes had a clear, intelligent expression, too mature and sad. The back of the eye was normal; there was no stasis of the papilla (eye-section of the hospital). The voice was deep and somewhat rough, often rising to a squeak, as in the case of a boy at the time of change of voice.

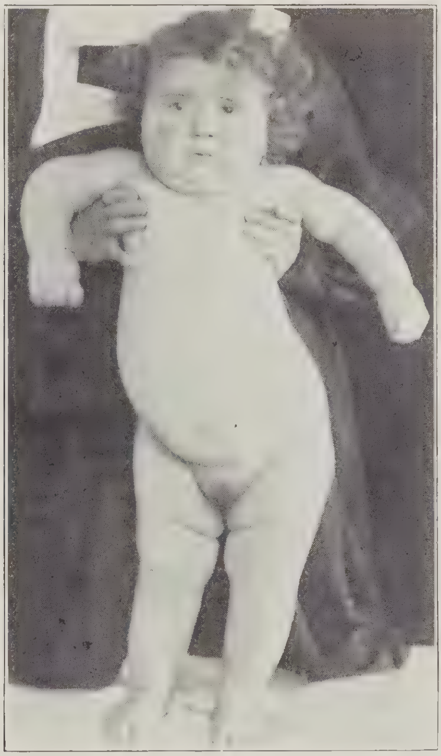

Fig. 1.—Appearance of patient.

By indirect laryngoscopy (Prof. V. Uchermann), it was seen that the vocal chords were unusually long and broad, almost as in an adult man. They were whitish, without essential injection, and closed well. No tumor was found. The neck was short and thick; the trunk was large in all dimensions; the extremities were short and thick, especially the thighs. The hands and feet were somewhat large, but well formed. The skin, except for the face, was soft and elastic, with strongly developed panniculus adiposus. On the cheeks, the skin was much reddened and sore, with a few short hairs. There was no abnormal pigmentation. There was a marked growth of hair on the labia majora and mons veneris, with a horizontal boundary above (Fig. 2). The hairs were up to 3.5 cm. long. On the thighs, shoulders and back, and partly on the front of the trunk, there was seen a dark growth of hair up to 1.5 cm. long. There was no axillary hair.

Genitalia: The labia majora and mons veneris were well developed. In place of the clitoris, there was a penis-like organ about 1.5 cm. long (Fig. 3). It was covered on the front by a prepuce, which extended into the labia minora. When the prepuce was drawn back, there was seen a quite well-developed gland with corona in which there was plenty of sebum. There was no urethral opening on the peniculus, but on the under side there was a longitudinal furrow. The corpora cavernosa urethrae could be felt. There was some degree of volume change.

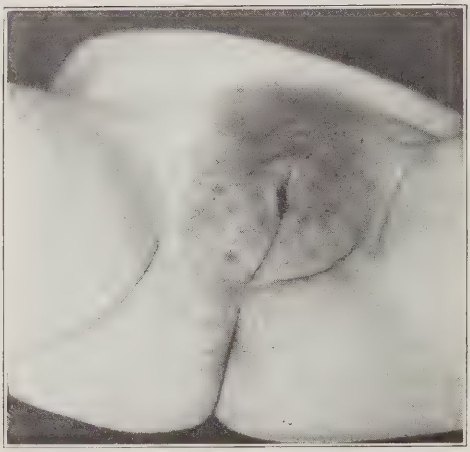

Fig. 2.—Growth of hair on genitalia.

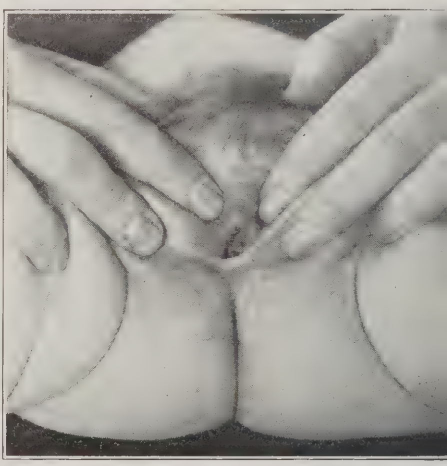

Fig. 3.—Development of genitalia.

The urethral orifice was found in the usual place. Catheters were easily passed into the bladder. The hymen was normal and the vagina was about 5 or 6 cm. deep. By means of the speculum, the portio of the uterus, with normal orifice, was seen.

Through the rectum, the uterus was felt. Its length was about 3 or 4 cm., the breadth 1 cm. The thickness of the organ was normal. No prostate could be felt, nor adexa. There was no indication of mammary glands. There were a number of small lymphatic glands on the neck.

No abnormality of the thymus and thyroid could be noted, and the sella turcica, under roentgen rays, seemed normal. In the throat and heart there was nothing of note. In the lungs, there was the sound indicative of bronchitis. The abdomen was large, with a small umbilical hernia. The liver reached three fingers' breadth in front of the costal arch; the spleen could not be felt. Because of the clinical picture, we now sought for a suprarenal gland tumor. The right kidney was palpable but seemed normal. Under the left arch of the ribs, we thought we could feel a tumor connected with the kidney. The surgeon, Dr. Backer-Gröndahl, confirmed this finding, and gave the following description of the condition: In the deep part under the left arch of the ribs a tumor with slightly knotted or rather twined surface was felt. Especially noticeable was a curling projection, the size of an almond. The boundary above could not be reached; laterally, it seemed the boundary was somewhat evenly bent and longitudinal. Downward it had a comparatively sharp side, extending a little from above and from the outside inward and downward to the quite palpable knot, which likewise formed a downward point. The tumor extended down until it was level with the point of the costa. It lay rather deep, but was not ballotable, as the hand could not reach high enough up at the back. Below this tumor, under a lower boundary, was felt another body which lay somewhat deeper, had a smooth slippery front and a smooth outward-bent side, and ended downward in an arch. The consistency and form reminded one of a kidney, about 4 or 5 cm. long, whose upper one third loses itself under the tumor. This was not ballotable, as it seemed to lie a little too centrally. None of the tumors were moved by the respiration. They could be pushed up and down a little. There was no soreness.

Bones: The head bones were firm; the fontanel was closed, and there was no raising of the epiphyses and no swelling of the ribs. There were sixteen teeth. The pelvis measurement, interspinal, was 14.5 cm., intercistal, 15.5 cm.; that is, a masculine type. The roentgenogram of the wrist showed that it corresponds to the wrist of a 3-year-old child. The body functions were normal; the temperature was normal. In the urine, which was as clear as water, there were no abnormal ingredients.

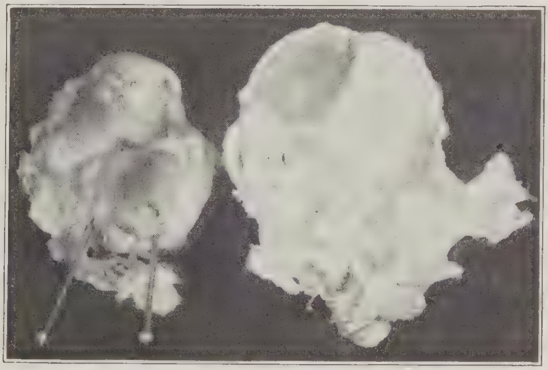

Fig. 4.—Appearance of tumor.

Blood: The blood test revealed (Sahli 71): polymorphonuclear neutrophils, 33 per cent.; small lymphocytes, 48.33; large lymphocytes, 5.67; large mononuclears, 10.8; eosinophils, 2.67; mast cells, 0.33. There was nothing of note in the red blood corpuscles (L. Dedichen).

When, as in the present case, abnormal hair growth, marked body development and premature development of the secondary sex characters are associated, one must bear in mind the pathologic function of three organs; namely, the pineal gland, the sex glands and the suprarenal cortex. A disfunctioning of the pineal gland is due mostly to a growth, as a rule teratoma. Our patient, however, offered no sign of brain tumor or any striking growth in length such as is seen in those tumors with which premature sex development comes relatively late; contrary to conditions as found in our patient. It may also be of interest to mention that Boehm found twelve cases of pineal tumor, all in *boys*. The sex glands in our case could not be felt, but we found a tumor in connection with and above the left kidney.

The hirsuties or virilism in question was therefore supposed to be due to a tumor of the suprarenal gland cortex. The question of operation now arose, but both Prof. P. Bull and Dr. Backer-Gröndahl considered the risk too great at so early an age and preferred to wait a year. We let the matter rest, as the child's good general health, as well as the slow growth of the tumor, pointed to its mildness. Thymus tablet treatment was instituted, and the child was sent home, Oct. 10, 1920.

I then wrote of the case to the head physician at Aalesund Hospital, Dr. Brekke, and, on the basis of our findings, and as on examination he also found a tumor, he determined to operate on the child.

Second Admission.—The patient entered the Aalesund Hospital, May 20, 1921. In the meantime, she had taken about 100 thymus tablets. In the opinion of the mother and others, there had been an improvement in the child's appearance since her stay in the State Hospital, especially after a severe throat attack with fever in December, 1920. The child could now walk and talk; she was not so fat, and some hairs on the face, and perhaps also on the mons pubis, had fallen out. The voice was just as deep.

A photograph, taken in April, 1921, seems to confirm this opinion. Dr. Brekke found the child certainly very large, but otherwise not striking, apart from her voice and the abnormal hair growth. She had as before sixteen teeth, and the tumor did not appear to have increased.

The day after admission to hospital, Dr. Brekke made an incision over the left groin and through it felt both ovaries, tubes and uterus, which all appeared normal. The left ovary, which was brought forward in the incision, looked normal, it being the size of a bean, oblong, whitish, hard and slightly indented in the middle.

Operation.—Five days later, the tumor was removed through an incision in the region of the kidney without bleeding. The patient was under ether for thirty-five minutes. The kidney was normal, with no connection with the tumor. The latter lay high up, and extended to the columna. The patient recovered quickly and was entirely well in a few days. The temperature rose to 102.6 F. (39.2 C.) the first evening but soon fell to normal. The tumor was sent to Professor Harbitz, in Christiania, who kindly placed at my disposal the result of his examination, including drawings of the microscopic dissections. "The specimen, a 3.5 by 2.5 by 2.2 cm. irregular curled tumor, weighing 10 gm., presented a surface covered with fibres of varying thickness. The consistency was somewhat variable, in part quite firm, in part soft. The surface of the cut had a lobed, complex appearance, divided into rounded compartments of different colors and appearance (Figs. 5 and 6). In several compartments, one could see a soft, homogeneous, red-brown growth tissue; in others, by the side of the first, a homogeneous yellow-gray center surrounded by a 2 or 3 mm. broad necrotic yellow-white area. In these compartments, lime was embedded. A number of smaller divisions, up to the size of a pea, had a yellow-white, almost cheeselike appearance.

"*Microscopic Examination* (Professor Harbitz).—The surface of the tumor was to a great extent covered with fibrous, partly hyaline degenerated tissue. Along the periphery, a brim of the original suprarenal substance was seen. Only a small part of the cells here were recognizable, as the suprarenal gland cortex

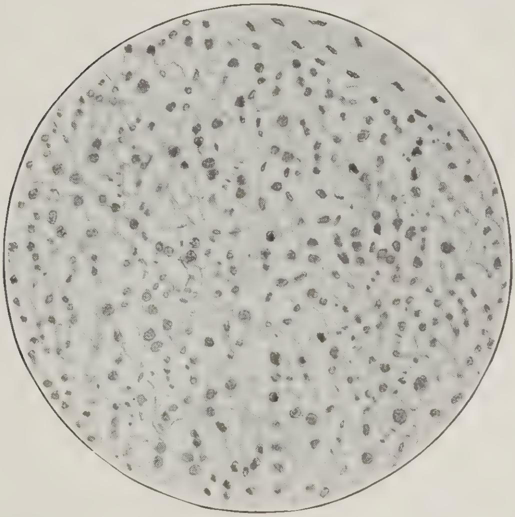

Fig. 5.—Cross-section of hypernephroma, showing regular structure.

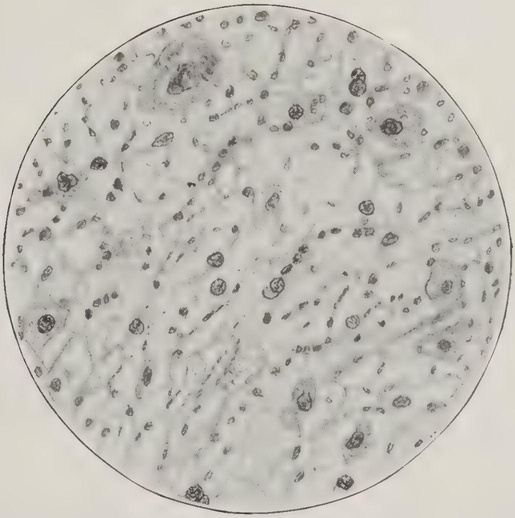

Fig. 6.—Cross-section of hypernephroma, showing irregular cell forms.

cells were arranged in clumps and strings. For the greater part, this tissue was infiltrated with cells resembling lymphocytes. There was also a diffuse fibrous area of neoplasia together with some bleeding in this tissue. The remains of the suprarenal glands above mentioned were found around large parts of the periphery of the tumor and in two diametrically opposite places. Besides the shell of suprarenal tissue above mentioned, which forms more obvious compact masses, there was also in this fibrous inlying capsule, in a long strip, small cell hoops of suprarenal epithelium, which gradually became unrecognizable. No extension into the distinct suprarenal gland marrow was seen. On the contrary, there were in the fibrous tissue in a few places clumps of a partly more compact and partly perforated tissue. Here also was found a markedly cellular and small-celled fibrous tissue, a part divided by fine meshes of fibrous tissue with large epithelium-like cells (Figs. 5). There was no sharp boundary between these two portions. The last mentioned parts showed cell forms of the type found in the large protuberances of which we shall speak later. The actual cellular, soft parts of the tumor were formed of a loosely built polymorphous-cell tissue. Among the cells, there was a small number of undifferentiated globular intercellular substances. The cells were of various kinds:

"1. There were numerous large spreading polymorphous giant cells and with one large nucleus or up to from eight to ten smaller nuclei. The protoplasm was bright-red (eosin). The large nucleus was rich in chromatin, and had, partly, a bladder-like appearance. In a specimen, sudan-stained, it was proved that the nuclei contained fat.

"2. By the side of the giant-cells were seen, as the most essential cells of the tumor, smaller, slightly polymorphous, well limited and distinctly epithelial cells with round nuclei. These cells partly resembled suprarenal cortex cells (Fig. 6).

"3. As a third type were found small spool-shaped fibrous tissue-like cells. These partly formed a net in the growth tissue, and partly appeared as a more distinct portion of the tumor.

"4. Spread out in the tumor tissue and somewhat unevenly divided were small lymphocyte-like cells. The form and size of the nuclei were somewhat variable.

"By the side of these there were found undoubted lymphocytes, partly in the growth tissue, partly in the adjacent granulating tissue.

"The yellowish white necrotic compartments and inlying lime particles appeared under the microscope only as a dull, degenerated structureless mass with lime sediment. The lime sediment was also found in the fibrous tissue on the outer part of the specimen. On the whole, these larger knots were built up of a scanty stroma, with the embedded large masses of cells probably of epithelial origin but rather polymorphous, especially in the oldest follicles. In the slightly degenerated, apparently younger follicles, the cell type had a distinct likeness to the suprarenal cortex. The tumor was confined by a thin shell of normal cortex which in some places, extending inward, was lost in the real growth tissue. The tumor itself consisted mostly of well-defined follicles filled with epithelial cells, which to a less degree resembled the suprarenal cortex (Fig. 5), but in the largest and the most numerous parts showed polymorphous large, multinuclear cell forms, even large giant cells (Fig. 6).

"However, there were found all intermediate forms in the epithelium mentioned. Judging by their formation, there was reason to consider these cells as chromaffin cells from the suprarenal marrow; but taking everything into consideration, it seemed most reasonable to consider the tumor as developing from the cortex, as a typical hypernephroma of rather long standing, as shown by degeneration and necrosis. On the whole, the tumor agreed in its structure fairly well with the suprarenal tumors found in similar cases described and illustrated by Glynn (1921).

"The structure, and not the least the small cast-off parts of the suprarenal cortex in the side of the tumor, suggested not a little a case of multiple tumor as described by Harbitz,[17] a hypernephroma in a kidney, a chromaffin tumor in the region of the suprarenal gland, a similar tumor in the region of the kidney, together with, finally, a cystadenoma in the pancreas in a 47-year-old man, who however did not show any disturbances in his development."

Later Examination (July 27, 1922).—The child's appearance was strikingly improved, the face being far less bulging, without an abnormal growth of hair. The skin was smooth and fine, appearing more childlike. All abnormal hair growth had disappeared except scanty, short, dark hairs on the labia majora. The labia and mons pubis were less projecting than before. The peniculus was perhaps somewhat smaller. The whole body, especially the abdomen, was less fat, and the umbilical hernia was smaller. The voice was deep, with changes to treble as before, but not hoarse. The child ran about in a lively fashion, talked well and was intelligent. She was nervous and at times depressed.

May 4, 1923: The height was 109 cm.; weight, 20.5 kg. There was still some hair on the labia. The child was lively and intelligent. Her voice was as before.

COMMENT

The tumor—the cause of the masculating process—must in the present case have arisen in the later part of the fetal life, at a time when the sex organs are nearly but not quite formed (urethral furrow on peniculus) perhaps in the fifth or sixth month. As evidence of this fact, the tumor proved to be of relatively early origin, as it was infiltrated with lime (lime-atrophy). Whether the mother's nervous shock in the early months of pregnancy had a casual connection with the formation of the tumor cannot be determined. The patient presented the picture of a partial hermaphrodism (Lipschütz) or, if you will, a feminine pseudohermaphrodism, and presented, according to Apert's classification of hyperepinephry, the type for the fetal period, that form which Gallais calls "le pseudo-hermafrodisme surrénal." Apart from the urethral furrow, the case represented in all respects more nearly his "virilisme suprarenal," in which the injury occurs after birth. With regard to the course, the obvious stoppage in the development of the virilism, which occurred especially after a severe throat affection, and the improvement which her relatives apparently observed in the last months before the operation, are of interest. If such a stoppage or improvement really took place, it could be explained by the thymus therapy, which in my opinion is not very reasonable, or through the quite extensive hyaline degeneration and calcatrophy in the tumor, which may have entailed a decrease of the secretion of masculine hormones. This latter explanation might find support in the circumstance that the tumor does not appear to have grown from September, 1920, to May, 1921; that is, for eight months.

After the operation, I noticed an essential improvement in the patient's condition, so that the influence of the tumor was not doubtful.

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[17] Harbitz: Tumors in the Sympathic Nervous System and in the Suprarenal Medullary, Norsk Mag. f. Lægevidensk., No. 1, 1915.

While all signs of virilism have not yet disappeared, even after two years (May, 1923), the condition is all that could be reasonably expected as far as several symptoms are concerned.

The voice, for example, will scarcely become more childish, as the larynx cannot be supposed to have the plasticity necessary for it to decrease in size. The hypertrophy of the clitoris will probably decrease, but the urethral furrow will remain.

On the contrary, ossification will certainly by degrees come to correspond to the age, and the pelvis will probably attain normal dimensions.

The hair growth is easily influenced; therefore, as might be expected, the hirsutism almost vanished soon after the operation. However, there is still a scanty growth on the pubes. Perhaps this is unimportant, but one cannot overlook the fact that there may be a hyperplasia of the right suprarenal cortex. It must be noted that the right kidney is palpable, which is not usual at that age.

It may indeed also be thought that other endocrine organs enter into the question.

The prognosis for our patient attaining adult age is good, if the disposition to tumor does not lead to the development of tumors of a malignant type.

Judging from the literature, our patient is the first child with the genitosuprarenal syndrome who has survived removal of the tumor. So much the more interesting will it be therefore to follow her future. Hijman's 3-year-old patient, a girl, died from shock; Linser's, a 5-year-old boy, after an exploratory laparotomy. Schiff's [18] patient, a 2-year-old girl; Dobbertin's, a 14-months-old girl, and Adam's, a 14-year-old boy, died shortly after the operation. There is therefore every reason to congratulate Dr. Brekke on the good result of his operation.

Without the operation, in all probability the child would at an early age have developed into a short overly fat, bearded woman. Perhaps one cannot, however, with the quiescent period of the disease in mind, quite disregard the possibility that the tumor might have ceased to grow and entirely atrophied, and that there might have been a spontaneous return to health.[19]

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18. Schiff, Erwin: Frühzeitige Entwickelung der sekundären Geschlechtskarakteristiken bei einem zweijährigen Mädchen infolge eines Hypernephroms der rechten Nebenniere, Jahrb. f. Kinderh. **87:** 519, 1918.

19. An extensive bibliography is found in Gallais (1914).

THE TEETH IN CHILDHOOD*

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The prevention of disease and the early recognition of physical and mental defects have long been the pride of pediatricians; the same should be true of the prevention of mental disease and the early recognition of dental defects. More and more parents are bringing their children to the physician with the request that routine physical examinations be made to see if the child is normal, and he then has an opportunity which may not be afforded the dentist until much later. Unfortunately, in the "complete" examination, the teeth are often overlooked. The responsibility for the prevention of dental disorders rests as much with the physician as with the dentist, and more especially with the pediatrician, who alone has ample opportunity to study the teeth of the child, and can often refer to the dentist children who might not otherwise be taken to him.

In the recognition of anomalous dentition, a familiarity with the time of eruption of the permanent teeth[1] is important. The curves in Figure 1, devised by Lyons and myself, represent the limits in the time and the average time of the eruption of the permanent teeth in 3,000 children between the ages of 5 and 13 years, observed in Rochester and in Olmsted County. The number of teeth erupted are charted in three-month periods. It will be seen that there is a marked irregularity in the time of eruption. For example, in one child, all four 6-year molars may have erupted by the age of 5 years; whereas, in another, they may not be in place until 7 years and 9 months, the average time of eruption being at the age of 6 years. Again, all twenty-eight permanent teeth may have erupted as early as 9 years and 9 months, or may not be in place even at the age of 13 years, 12 years being the average age for full eruption. In a larger series, there would, in all probability, be a few cases showing more premature eruption of the permanent teeth.[1]

Figure 2 shows the line given in dental textbooks to represent the time of eruption of the permanent teeth. The mean of the average time of eruption in our series indicates earlier eruption, probably because we have charted the time in three-month periods instead of one-year periods,

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* Received for publication, Nov. 26, 1923.

* From the Section on Pediatrics, Mayo Clinic.

[1] James, W. W., and Pitts, A. T.: Some Notes on the Dates of Eruption in 4,850 Children, Aged Under 12, Proc. Roy. Soc. Med. **5**:80-101, Pt. 3, Sect. Odont., 1912.

or possibly because the permanent teeth are erupting earlier than formerly, as a result of dental caries and early loss of the deciduous teeth.

Not only is there a variation in the time of eruption, but there is also a marked variation in the order of appearance of the different permanent teeth.[1] The first permanent teeth are the 6-year molars, which come in distal to the temporary molars. These are rarely recognized as permanent by the parents and often not by physicians, and are, therefore, allowed to decay. It is the duty of every pediatrician to point out these teeth to parents, so that measures may be taken for their preservation. The next teeth to appear are the lower central incisors, which are followed closely by the upper central incisors. Occasionally they appear coincident with, or prior to, the 6-year molars. The lower and then the upper lateral incisors are next in order. After the 6-year molars and the incisors are in, there is no more orderly eruption. Usually, there is a tendency for the corresponding mandib-

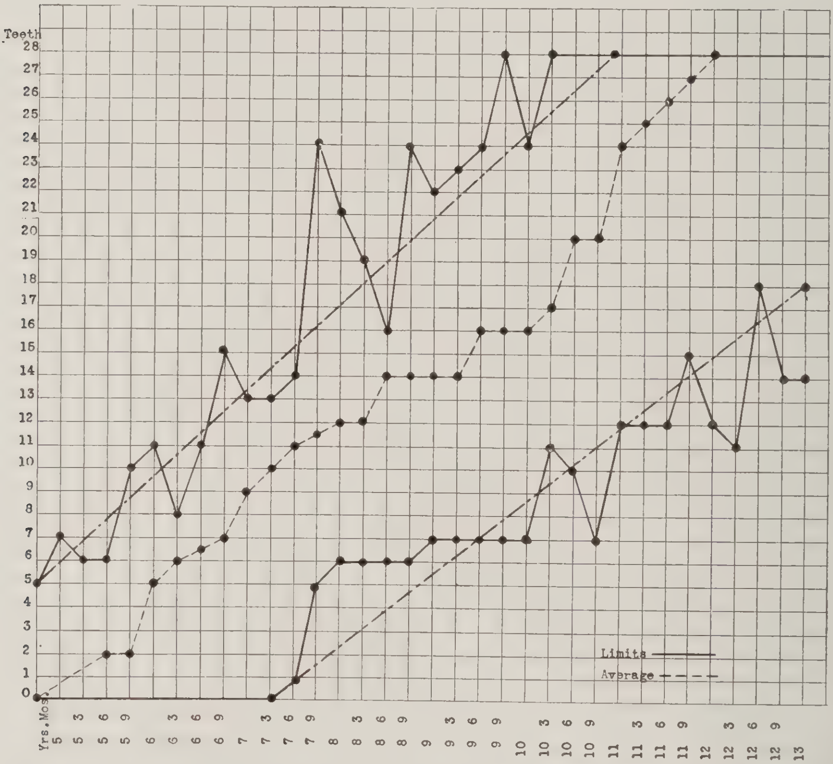

Fig. 1.—Erupted permanent teeth charted in three-month periods. The curves show normal limits and average time of eruption.

ular teeth to erupt prior to the maxillary ones. The first bicuspids usually erupt in order after the incisors. These are followed by the second biscuspids, and then by the canines or the second molars. The mandibular canines often erupt in order after the lateral incisors. The time of eruption of the permanent teeth seems to have a definite relation to the decay and premature extraction of the deciduous teeth.

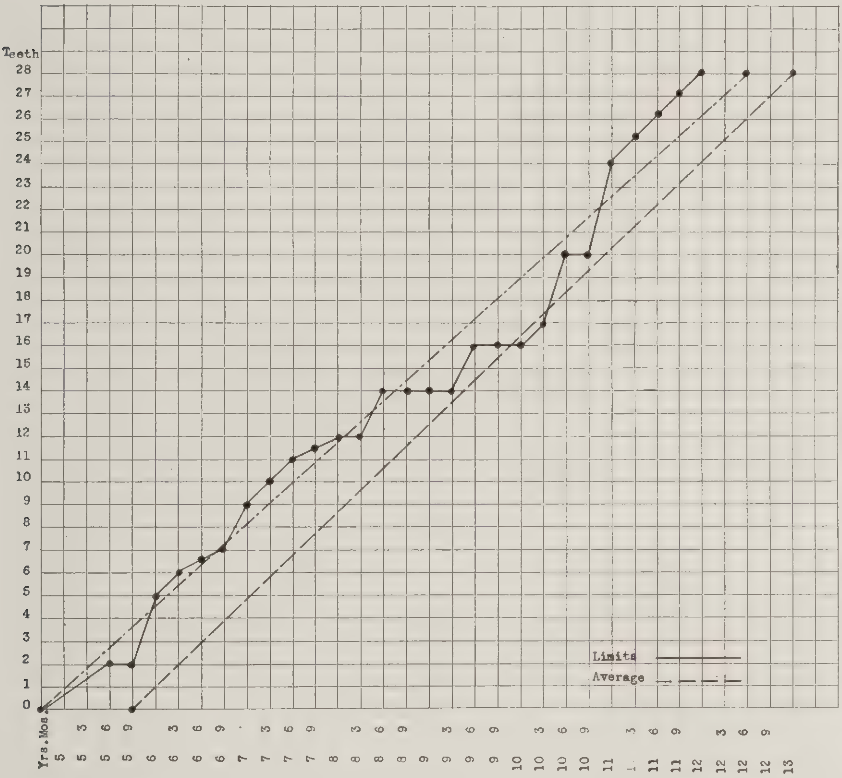

Fig. 2.—Erupted permanent teeth charted in three-month periods. The curve shows the average time of eruption. The upper dotted line represents the mean of this curve; the lower dotted line, the average time of eruption usually given in dental textbooks.

If the deciduous tooth is lost early, there is a tendency for the corresponding permanent tooth to erupt early.

The recognition of malocclusion early in childhood is of vital importance.[2] It is wise always to count the teeth and to notice whether the space is wide enough to allow each tooth to erupt. Between the ages of 4 and 4½ years, the temporary teeth should begin to show a certain amount of spacing, especially in the incisor group.[3]

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[2] McCauley, C. M.: Preventive Orthodontia, Internat. J. Orthodontia **7:** 529-533, 1921.

There are two schools of orthodontia. The members of one school believe in the early treatment of any malocclusion which is present, or imminent.[4] If possible, they prefer seeing the child prior to the age of 4 years, when, by examination, they can detect early pathologic lesions, and by means of the roentgen ray see anything unusual in the unerupted permanent teeth.[5] Deformities of the maxillary denture due to thumb-sucking; those coincident with nasal stenosis from tonsils and adenoids, and those due to premature loss of deciduous teeth can be beneficially treated at this time.[6] If treatment of the deciduous or early permanent teeth is begun early, while the bones are pliable, simple devices are effective, and the periods of treatment short, although, of course, long observation is necessary to avoid recurrence.

Orthodontists of the other school believe in later treatment, after the bicuspid teeth are in place, which is usually after 10 years of age, when the parts are less pliable, and apparatus must needs be more cumbersome and be retained for months or years. It is strange how firmly the idea has become fixed in the minds of physicians and the laity that the time for orthodontia is at the age of 12 or 13 years. If put off until this time, it is usually postponed for life. It is clearly the duty of the physician to assist the orthodontist to map out this plan of treatment as early as possible; however, early interference with the temporary dentures is not advisable unless the condition has arisen from some local cause which nature will not correct.[6]

The common cause of malocclusion is the early loss of the deciduous teeth from decay, and this is largely preventable.[3] Inherited forms of malocclusion represent only an exceedingly small percentage of cases.[7] Ten per cent. of the 3,000 children observed were found to have serious malocclusion, and 50 per cent. had moderate malocclusion. According to Lyons, 65 per cent. of 267 children between 5 and 15 years of age passing through the dental department of the Mayo Clinic had malocclusion, 85 per cent. of which was due to the early extraction of deciduous teeth. When one realizes that not even 1 per cent. of the patients with severe malocclusion ever receive orthodontic treatment, the importance of prevention by preservation of the deciduous teeth until the time of their normal exfoliation is evident.

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[3] Kregarman, S. L.: Prevention Versus Treatment of Malocclusion, Internat. J. Orthodontia **6**:222-229, 1920.

[4] Bogue, E. A.: Early Treatment of Malocclusion, Internat. J. Orthodontia **8**:119-128, 1922.

[5] James, W. W.: A Theory of Eruption, Internat. J. Orthodontia, **9**:676-683, 1923; McCauley: Footnote 2.

[6] Case, C. S.: Etiologic Influences of Deciduous and Erupting Permanent Teeth, with Principles of Treatment, Internat. J. Orthodontia **7**:131-137, 1921.

[7] Chapman, H.: Orthodontics: The Bearing of Etiology on Treatment, Internat. J. Orthodontia **9**:93-119, 1923.

INHERITED DENTAL ABNORMALITIES

There are certain inherited dental abnormalities which it is important to recognize and which usually affect only the permanent dentition. Congenital absence of any permanent teeth may occur. Absence of one or both upper lateral incisors is the most common. Extraction of the tooth opposite the absent one, although not always necessary, is one of the few instances in which extraction is justified in the treatment of malocclusion.

Impaction also occurs commonly, most often in the bicuspid group, although any tooth may be impacted. It may occasionally be an inherited abnormality, but it is usually acquired, and is the result of crowding due to the too early loss of deciduous teeth. The 6-year molar may be impacted against the deciduous molar, but usually, if missing after 7 years of age, it has been prematurely extracted. The canine tooth is variable in its time of eruption and is prone to appear in an anomalous position. If there is space for it, it will tend to come into normal occlusion, but as this space is often compromised, it is commonly out of occlusion. Other inherited dental abnormalities are bifid bicuspids, pegged lateral incisors and short, broad upper incisors with long, narrow lower ones.

APLASIA

Various forms of aplasia occur in the permanent teeth. A number of children, both in the schools and in the Mayo Clinic, have been seen with the so-called collar and sleeve deformity. In this type of aplasia, the upper half of the crown is defectively enameled and is often a mere jagged stump. The mulberry molar is a manifestation of this condition in the 6-year molar. The 6-year molar and the incisors seem almost always to be involved when this deformity is present. In one case, the upper lateral incisors were not affected (Fig. 3). The first bicuspids and the canines have also often been affected. In this series, the second bicuspids and the second molars were not affected. A similar deformity in the deciduous teeth was observed in only one child, in whom all four canine teeth were involved, and the lower incisor teeth showed caries about the roots, only the roots of the upper incisors remaining intact (Fig. 4). Such aplasia was present in 0.5 per cent. of 3,000 children examined.

Defective enamelization in the form of multiple pitting was less common. The cause of this form of aplasia and of the collar and sleeve type is unknown. All of the children seen at the Mayo Clinic had negative Wassermann reactions, and none of the children seen in school had any stigmas of hereditary syphilis. If the sleeve and collar deformity is seen in cases of hereditary syphilis, it must mean that it is a coincidence, or that a variety of causes have acted to produce the condition. It has also been attributed to exanthematous diseases, but in the case shown with involvement of the deciduous teeth, such could not have been the case; for the crowns of these teeth were fully formed prior to birth.[8] In other cases, we have been unable to get any history of contagious diseases. These children are usually healthy and normal in other respects. Although presumably some infection must be the causative factor, the specific infection, selective localization and comparative rarity of the condition is still unsolved.

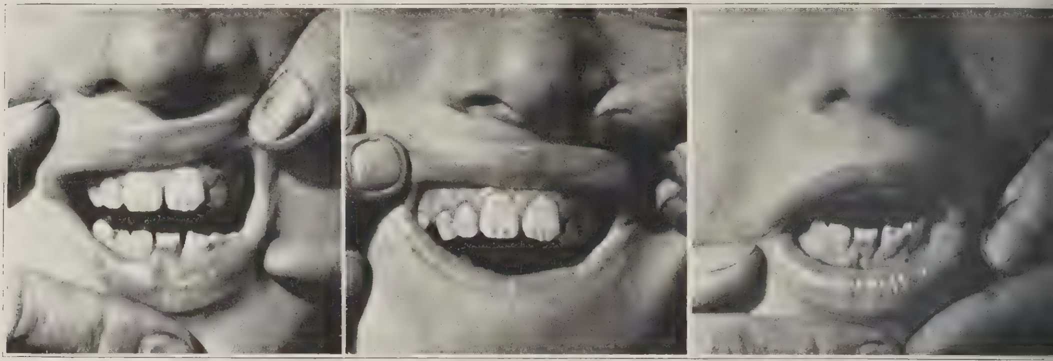

Fig. 3 (Patient, aged 12 years).—Appearance of front teeth. There were eighteen permanent teeth, with collar and sleeve deformity of 6 year molars, four lower incisors and two upper central incisors. The other teeth were normal. The patient had had measles, parotitis, diphtheria, pertussis and a discharging ear. The general health was good, the weight, normal. There were no signs of rickets, and the Wassermann reaction was negative.

FIFTH CUSP

Another phenomenon about which there is much confusion in the literature is the presence of the so-called fifth cusp. This is simply an atavistic remnant and is of no significance.[9] In a large series of cases, it was found to be present in 50 per cent., whether the child was normal or was suffering from divers ailments. The upper deciduous molars and the upper 6-year molars were the teeth presenting this cusp. It is occasionally unilateral; is rarely seen on any other tooth, and is extremely variable in size and appearance. Sometimes, it is merely a tiny projection on the surface of the teeth; again, it may be as large as any of the four other cusps of which the tooth is formed. Its presence probably has no relation to the child's general health, or the condition of the teeth, although it has often seemed that such a tooth is unusually sturdy and strong. The absurd use of mixed treatment and other forms of antisyphilitic treatment on the theory that this is a syphilitic manifestation has no foundation.

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[8] Blay, C. P.: The Care of the Teeth in Relation to Motherhood and Infancy, abstr. Internat. J. Orthodontia **6**:194, 1920.

[9] Baudouin, M.: Anatomical Demonstration of Atavistic Origin of Fifth Cusp, abstr. Internat. J. Orthodontia **6**:331, 1920.

SYPHILIS AS A FACTOR IN MALFORMATION

A study of the permanent upper central incisors has also been made. It was found that in 12 per cent. of children digitations were present, regular and of full height. In 48 per cent., the digitations were slight or absent, and the biting edge of the tooth was straight and even. In 40 per cent., the digitations were irregular or the biting edge was irregular and uneven (Fig. 5). It is this last group of 40 per cent. which is so often wrongly spoken of as suggestive Hutchinson's teeth. Furthermore, 12 per cent. were found to have convergent sides which might simulate the so-called chisel-shaped teeth of hereditary syphilis. The anteroposterior thickening, so common in the typical permanent upper central incisor of hereditary syphilis, was rarely seen in nonsyphilitic patients. From these observations and the observation of the teeth in many cases of hereditary syphilis, it would appear that the concavity on the biting edge, the anteroposterior thickening and the convergent

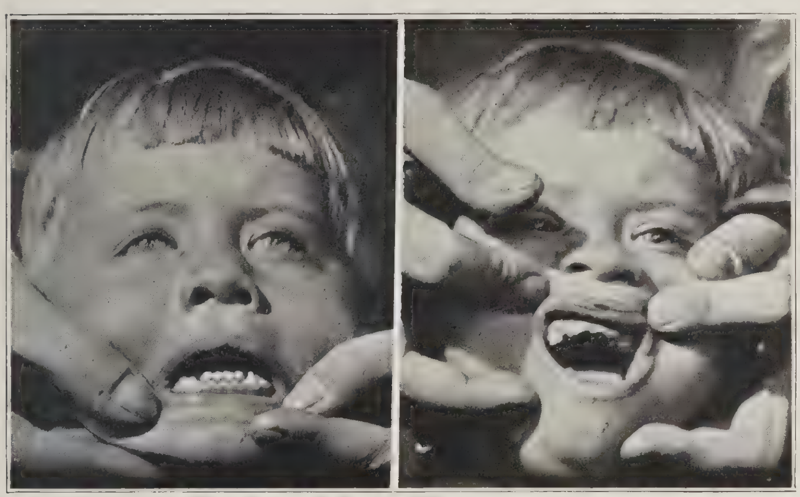

Fig. 4 (Patient, aged 2½ years).—Appearance of front teeth. There were twenty deciduous teeth. The four canines only showed collar and sleeve deformity. The upper right and lower left molars and all lower incisors showed deficient enamel on the anterior surface. Only the roots of the upper incisors remained. The patient had pneumonia at the age of 1 year. There was marked prominence of the occiput. The child was 16 per cent. underweight. The Wassermann reaction was negative.

and often convex sides, all taken together, and applying only to the upper permanent incisors, are the only dental signs which are pathognomonic of hereditary syphilis. If there is the shadow of a doubt about the teeth being Hutchinson's, they are usually not. The deciduous teeth are never pathognomonic, and no authentic case of Hutchinson's teeth in the deciduous incisors has ever been reported. The pegged or chisel-shaped permanent upper lateral incisors are an inherited abnormality and not pathognomonic of hereditary syphilis. Stokes and Gardner report a case of hereditary syphilis in which Hutchinson's teeth were diagnosed by roentgen ray prior to their eruption.[10] Such a diagnosis is only applicable after the permanent crowns are fully formed. It is, therefore, valuable confirmatory evidence in cases of suspected syphilis prior to the eruption of these teeth. However, in only a small percentage of cases of hereditary syphilis are

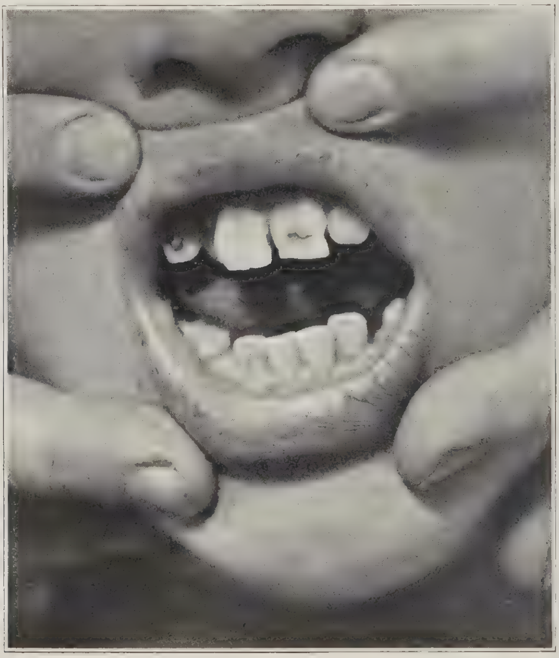

Fig. 5 (Patient, aged 10½ years).—Appearance of front teeth. There were fourteen permanent teeth. The anterior surfaces of the permanent upper central incisors were irregular and discolored. The lower one fourth of the crown was thin, and narrower than the upper three fourths. The digitations were irregular on the right and absent on the left. The patient had had measles only. A marked funnel chest and scaphoid scapulae were noted. The patient was 16 per cent. underweight. The Wassermann reaction was negative.

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[10] Stokes, J. H., and Gardner, B. S.: Demonstration of Unerupted Hutchinson's Teeth by the Roentgen Ray, J. A. M. A. **80**:28-29 (Jan. 6) 1923.

Hutchinson's teeth present, so that other more constant signs, a suggestive history and a laboratory investigation are more valuable in the diagnosis.

DENTAL CARIES

The question of dental caries is most vital to the physician and to the patient. As is well-known, caries is most prevalent in infancy, childhood and adolescence, and it is in these periods that prevention must be practiced.[11] In infancy, this consists mainly in the prevention of malnutrition and underfeeding in elements necessary for building dental structure.[12] Frequent and systematic observation and cleansing of the teeth from the time of their eruption are essential, and cleansing of the teeth by proper food at the end of each meal is preferable to the use of the tooth brush.[13] Thumb sucking, with its resultant malocclusion, should, of course, be guarded against. If it has caused irregularity of the maxillary denture, daily pressure should be employed to correct this deformity. Although breast-feeding is, of course, the ideal feeding, it is not essential in the prevention of either caries or malocclusion. If infants are properly fed artificially and normal nutrition is maintained, normal development of the teeth and jaws will result. The control of the nutrition and diet of the mother during pregnancy is important.[8] If lancing of the gums in infancy should become necessary, it should be done by the dentist with the actual cautery.[14]

In childhood and adolescence, prevention of caries is largely dependent on the cleansing of the teeth and on the prevention of general infections. It is well known that the teeth often decay rapidly during and after febrile diseases. Much of this is due to the fact that during illness the teeth are not so likely to be kept clean, and that elevation of temperature causes any residual food on the teeth to decay more quickly and form a nucleus for beginning caries.[11] Conversely, it must be remembered that prevention of caries by the elimination of the teeth as foci may reduce the incidence of communicable disease.[15] Of course, the diet is as important during childhood and adolescence as during infancy, for the permanent teeth are being formed at the same time as the temporary ones are being maintained.[16]

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11. Millberry, G. S.: The Problem of Dental Hygiene in Children, Arch. Pediat. **33**:533-538 (July) 1916.

12. Talbot, F. B.: The Relation of Diet to the Development of Children with Special Reference to the Teeth, M. Clin. N. America **2**:1333-1340 (March) 1919.

13. Gibbs, J. H.: Child Welfare and the Prevention of Dental Disease, Edinburgh M. J. **18**:433-441 (June) 1917.

14. Barker, P. A.: Operative Procedure on Children's Teeth, J. A. D. A. **10**:527-534, 1923.

15. Clark, T., and Butler, H. B.: Children's Teeth, a Community Responsibility, Pub. Health Rep. **35**:2763-2779 (Nov. 19) 1920.

16. Mellanby: The Value of the Animal Experimental Method in Dental Research, Dental Rec. **42**:1-12, 1922.

How can the physician help to eliminate the occurrence of dental caries? The goal we seek is that no deciduous tooth be extracted until the corresponding permanent tooth is ready to take its place. This is normally at the time when the arch is large enough to support the permanent tooth in normal occlusion. Evidently, then, cavities should be filled when they are small.[14] However, it must be borne in mind that any deciduous tooth which is not devitalized can and should be filled. If the roots of deciduous teeth have not yet begun to be absorbed, even the root canals may be nicely filled.[17] In general, however, all devitalized teeth should be removed immediately, as they are a source of peril to the very life of the patient, and the maintenance of the normal arch becomes of secondary importance.[18] The pulps of deciduous teeth are larger in proportion to the size of the teeth than are those of the permanent teeth. Also the wall of dentin is thinner, so that slight decay is dangerous.[17] Therefore, a roentgen-ray examination of carious teeth is often necessary, if the proper treatment is to be instituted.

As regards the treatment of radial caries, the proximal decay can be cut away,[17] or the decay may be arrested by the application of strong silver nitrate solution.[19] The latter treatment is preferred by most dentists. I have seen teeth that were affected by radial caries beautifully filled by clever dentists.

Broken off incisors are common in childhood. If deciduous teeth are broken, decay should be arrested, if possible, and the teeth kept in place until time for the permanent teeth to erupt. Decay, if it occurs in the permanent teeth, should also be arrested. If the pulp is uninjured, the teeth can be built up after they have grown to be large enough so that lateral pegging can be done without injury to the pulp cavity. This can usually be accomplished about four or five years after the time of eruption of the tooth, or at the approach of puberty. If the pulp is injured, the broken-off, permanent teeth will have to be removed and replaced by artificial teeth at the time of puberty. It is important to remember that teeth can become devitalized by trauma which is not sufficient to break off any part of the crown. These teeth may or may not become black. The trauma may, and probably will, cause a root injury.

The importance of the sixth year molars should be emphasized. They are the keystones of normal occlusion in the mouth, and as such their preservation is essential.[3] When they first come in, they often have deep incisuras, which retain food easily. Early decay along these deep crevices in the crown is common. Prophylactic soft fillings can be placed in these crowns to advantage, even though decay has not begun.[17] When the teeth are full-sized and completely erupted, these fillings may be removed or allowed to wear themselves out. In this way, the permanent tooth, which is most subject to decay, will be saved, and the time of most prevalent decay will be safely passed.

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[17] Black, G. V.: A Work on Special Dental Pathology, Chicago, Medico-Dental Publishing Co., 1915, 489 pp.

[18] Perry, R. H.: The Medical Aspect of Dental Caries in Childhood, J. Tennessee M. A. **11**:257-264 (Nov.) 1918.

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SUMMARY

The pediatrician, because of his unique opportunity for early observation, should share responsibility with the dentist in preventing malocclusion, decay and infection in the teeth of children. If the physician will inform himself with regard to the normal and abnormal development of teeth, and in every routine examination of a child will observe the condition of its teeth and emphasize the importance of their proper care, much disease and decay will be avoided.

TWO CASES OF ACUTE EPIDEMIC ENCEPHALITIS OCCURRING IN ONE FAMILY *

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Since the beginning of the epidemic of acute encephalitis, many articles have been written regarding the question of contagion in this protean disease. Netter,[1] Stern,[2] Flexner,[3] Stiefler,[4] Wechsler,[5] Guillian and Lechelle,[6] de Laroche,[7] Lévy,[8] Fyfe,[9] Lemierre[10] and, recently, Hunt,[11] in a report of the 1923 New York epidemic, have contributed case reports to the literature or have summarized a large number of cases in which the element of contagion is freely discussed. This question is a very important one in the hospital management of the disease. The object of this paper is to report two cases of acute epidemic encephalitis occurring in one family. The fact that both of these cases developed under very poor hygienic conditions in which a family of five were living in the same room must be considered. All five members of the family were affected with an influenzal condition approximately at the same time.

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* Received for publication, Dec. 7, 1923.

* From the Neuropsychiatric Clinic, Philadelphia General Hospital.

* Read before the Philadelphia Neurological Society, Nov. 23, 1923.

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6. Guillian, G., and Lechelle, P.: A Case of Contagion in Lethargic Encephalitis, Bull. Acad. de méd. **84**:321 (Dec. 14) 1920.

7. De Laroche: A Case of Familial Contagion in Lethargic Encephalitic, Paris méd. **10**:364 (Nov. 13) 1920.

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9. Fyfe, L. L.: Encephalitis Lethargica; An Intensive Outbreak in a Small School, Lancet **2**:379-381 (Feb. 24) 1923.

10. Lemierre, A.: Familial Epidemic Encephalitis; Probable Transmission of the Virus by a Person Affected for Three Years, Bull. et. mém. Soc. méd. d. hôp. de Paris **44**:1628 (Dec. 31) 1920.

11. Hunt, E. L.: Epidemic (Lethargic) Encephalitis: the Recent New York Epidemic, J. A. M. A. **81**:1352 (Oct. 20) 1923.

REPORT OF CASES

Case 1.—M. M., girl, aged 13 years, in whom the onset of the present attack occurred in November, 1919, presented symptoms of a respiratory infection, with marked asthenia, many aches and pains and occasional vomiting. She was said to have had a cold in her head, also to have had a slight fever. On the second day, her mother noticed that her eyes were crossed, and she complained of double vision. For the next week, she showed typical findings of acute delirium, being very apprehensive and also having extensive visual hallucinations. She was in bed during this period of approximately two weeks. She was never lethargic, but suffered from marked insomnia with agitation at night. On getting up two weeks after the onset of illness, the patient developed choreiform movements, for which she had been treated for the past few years in various dispensaries. On the advice of a physician, she later had a tonsillectomy performed. In 1920, when she first reported to our neuropsychiatric clinic, routine physical examination revealed findings of a mitral stenosis. At this time, she showed typical generalized choreiform movements and was quite agitated. She was sent for a rest period in the country, where she remained for several months, until the choreiform movements disappeared. Neurologic examination revealed weakness of left external rectus, a unilateral ptosis, marked incoordination in finger to nose test, etc. On several occasions, she showed slight nystagmoid movements of the eyeballs. She frequently complained of diplopia. Otherwise, all examinations were negative. During the past year, she had shown no choreiform movements.

Secondary sex characteristics since puberty had been marked. She had been growing obese, but had not shown any behavior abnormalities in school, where her progress was normal. At home, she was very irritable, fussy, obstinate, sullen and quarrelsome, and showed a general emotional lability. No definite delinquent acts had been noted and behavior abnormalities for the most part had played an insignificant part as a sequel of the disease. During her last visit to the clinic, she had shown no evidence of incoordination of any description and apparently had been adjusting herself well to her surroundings.

Spinal fluid and blood examination, when she was admitted to the hospital, were all reported negative. Otherwise, the general examination was negative throughout.

Case 2.—E. M., girl, aged 11 years, slept with M. M., and developed practically identical symptoms a few days later, her main complaints being headache and dizziness. Her eyes crossed more than M. M.'s, according to her mother's report. She had diplopia and had had a persistent strabismus ever since. For brief periods, she was delirious at night, reacting on several occasions to visual hallucinations. She had no radiculitis at this time, and no choreiform movements, and there have been no sequelae of neuropsychiatric significance in this case. She had been getting along very well in school, progressing normally for her age. Her mother stated that frequently she complained of pains through her arms and legs for a year following this illness, but these had ceased entirely and she had no subjective complaints at the present time. There were no neurologic sequelae, except a left internal strabismus, which appeared to be constant. A heart specialist stated that there was no damage to the valves. Laboratory examinations were all negative.

It may be wise to review the mother's attack at this time. She is said to have had a very severe attack of influenza, with the findings of acute respiratory infection and delirium. Her main complaints were headache, dizziness and visual impairment. Since she recovered from this illness, she felt there had been a gradual change in her vision. The eye grounds are negative at present. There was no history of insomnia or lethargy. She had complained of occasional pains in her arms since this illness.

COMMENT

Many interesting facts are suggested in the study of the two cases. First, the family group is interesting, and a diagnosis of a postencephalitic condition in the two children appears most probable. There is some question about the mother having a similar illness. The fact that this developed following influenza is of interest in that we frequently have seen this relationship in other cases of encephalitis in children that we have studied. The statements in the literature seem to show that encephalitis frequently develops after influenzal conditions when the patient's resistance is lowered and he is most susceptible to a secondary invader such as may be present in the etiologic agent of acute epidemic encephalitis. Cases of this type suggest the latter possibility and confirm the reports of others in this regard. These two cases were the only ones seen by us in which encephalitis has occurred in two members of the family, in a large number of postencephalitic disturbances observed in both the outpatient clinic and the neuropsychiatric wards. The question regarding the transmittability of the virus causing encephalitis must be considered in the foregoing cases. Whether or not hospital isolation is essential will depend on further data. We do not practice isolation in our general hospital. No cases of hospital contagion have been reported in the literature, with the exception of those of Wechsler,[5] in which two interns in a hospital developed encephalitis. The rarity of instances of this type may well be looked on, therefore, as accidental. We feel that direct transmission in cases of encephalitis is almost negligible. Wechsler,[5] out of 864 cases found only five cases of the disease occurring in two members of the same family. This constitutes one half of 1 per cent. of the cases in which he has completed careful clinical statistical studies.

SUMMARY

In two cases of acute epidemic encephalitis in children of one family, the question of contagion and their relation to post-influenzal conditions were points of interest. The rarity of these instances suggests that they had better be looked on as accidental and that the factor of direct transmission in acute epidemic encephalitis, with the facts we have now at hand, is practically negligible.

KIDNEY DISEASES IN INFANTS AND CHILDREN

II. MALIGNANT HYPERTENSION NEPHRITIS: PRIMARY SCLEROTIC KIDNEY (SCHRUMPFNIERE) *

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In a previous paper,[1] we divided the cases of kidney disease seen by us into four groups, stating that the classification was based solely on (*a*) the clinical picture, (*b*) the duration of the disease and (*c*) the prognosis. We described the group called nephrosis, and now proceed to define another, which may be termed malignant hypertension nephritis in children. This group, of which we append three examples, is not very common in infancy and childhood, yet the picture is so clear cut that an absolute diagnosis and prognosis can be made.

REPORT OF CASES

CASE 1.—*History*.—S. G., a boy, aged 3½ years, of Russian parentage, was an only child. The father and mother both had positive Wassermann reactions, but, from the history of the father and the result of examination in the child, it seemed definitely established that the parental infection occurred long after the birth of the child.

The patient was supposed to have had measles, parotitis, diphtheria and scarlet fever. It was impossible to obtain the dates of these infections, and the accuracy of the information is not assured. Tonsillectomy had been performed a year previously.

Within the past four months, the child had complained of sharp pain in the epigastrium and right upper quadrant of the abdomen, occurring about one-half hour after meals. The pain had increased in severity and constancy, so that now it was present practically all the time. He vomited occasionally, but this did not relieve the pain. The vomitus did not contain blood. Constipation was marked. The child had had a voracious appetite and marked thirst for the past four months. During this time, he had nocturnal enuresis and passed large quantities of urine. He complained now of headache and felt weak and sick. He had had no dyspnea nor edema.

Examination.—The head was somewhat large and out of proportion to the body. The child appeared old and wrinkled, and the temporal arteries were plainly visible. The pupils reacted to light and in accommodation. The skin was brownish and very dry. The teeth were in fairly good shape. The tonsils had been enucleated. The pharynx was normal. The lungs were negative to auscultation and percussion. The heart's action was forcible. There was a faint systolic murmur, and a markedly accentuated second sound at the apex. The pulses wherever palpable were like pipe-stems—hard and noncompressible. The abdomen was soft and negative to percussion and palpation. The spleen was just palpable, and the liver was felt two fingers below the border of the ribs.

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* Received for publication, Dec. 7, 1923.

* From the pediatric department of Mount Sinai Hospital.

[1] Schwarz, Herman, and Kohn, J. L.: Nephritis in Children, Am. J. Dis. Child. **24**:125 (Aug.) 1922.

Blood pressure on admission was 250 systolic and 195 diastolic, and the Wassermann reaction of blood and spinal fluid was negative.

The blood examination showed erythrocytes, 5,200,000; leukocytes, 8,200; polymorphonuclear cells, 80 per cent.; and hemoglobin, 55 per cent. The phenolsulphonephthalein excretion was 56 per cent. in two hours.

Blood chemistry: The urea nitrogen was 16.8 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 50.3 mg.; uric acid nitrogen, 1.7 mg., and creatinin nitrogen, 1.3 mg. per hundred cubic centimeters of blood.

Urinalysis: A twenty-four hour specimen showed the volume to be 1,200 c.c. (with an intake of 800 c.c. of fluid); reaction, acid; specific gravity, 1,004, and a heavy trace of albumin. Microscopically, there were a few red and white blood cells.

Ophthalmologic examination (Dr. Julius Wolff): The nerve heads were red, and the margins obliterated and merged into the retina. An edema of one diopter was present. The arteries were narrow, fine, corkscrew vessels. There were fresh and old hemorrhages, and several spots of degeneration, especially in the region of the macula and the temporal side of the nerve head.

From the physical examination and the laboratory findings, we may deduce that the patient had markedly increased systolic and diastolic blood pressure, thickened arteries and moderate secondary anemia; no retention of nitrogenous products in the blood, a polyuria, and a urine of low specific gravity, with a moderate amount of albumin. The eyegrounds showed a typical neuroretinitis albuminurica.

Table 1.—*Fluid Intake and Urine Volume (c.c.)*

	Date											
	March				April						May	
	21	23	25	27	1	5	10	15	20	25	5	20
Intake....	550	950	855	1,520	750	800	1,200	1,100	1,400	800	1,100	200
Excretion	980	625	1,200	1,150	1,000	800	1,000	2,225	2,250	500	700	200

Patient moribund.

Course in Hospital.—The patient had been in the hospital two months when he died, so the entire course of his illness was about six months. During these two months in the hospital, the abdominal pain was constant and very severe. Benzyl benzoate, nitroglycerin and amyl nitrate were given without effect. During the last two weeks of the disease, the abdominal pain was even more marked, and there were large amounts of clotted blood in the stool. Roentgen-ray examination of the peripheral and abdominal arteries revealed no signs of calcification. The systolic blood pressure remained persistently high (around 200) during the entire time. The nitrogen determination of the blood serum repeated at three different periods showed no higher figures than at the first examination. The fluid intake and the urine volume can best be seen from the data presented in Table 1.

The specific gravity of the urine was always low, and microscopically a few hyaline and granular casts were occasionally seen. Death was due to inanition and hemorrhage. Necropsy was not permitted.

Case 2.—*History.*—K. L., a girl, aged 11½ years, whose parents and a brother and sister were well, gave no history of kidney disease in the family, nor personal history of any infectious disease, except measles and pertussis eight years before. The patient was in excellent health and had a good appetite until the onset of this illness.

For the past six months, the child had not been looking so well, but there were no definite symptoms of any kind until six weeks previously, when the patient had begun to vimit and to have abdominal pain. The pain was cramplike in character, and was located in the region of the umbilicus. The vomiting and pain continued every day, and often were present several times a day. In addition, the child had a marked polyuria, voiding often every fifteen minutes, and many times at night. There were no headaches, no disturbances of vision, and no cardiac nor other symptoms.

Examination.—The patient was fairly well developed and well nourished, and did not appear acutely ill. The nose and throat were in good condition, and the skin was normal. The lungs were normal to percussion and auscultation. There was visible and palpable episternal pulsation of the heart. The apex beat was seen and felt in the sixth interspace, 8.5 cm. from the midsternal line. A definite, soft systolic murmur was heard at the apex, which was not transmitted. Palpation and percussion of the abdomen were negative. The spleen and liver were not palpable. The extremities showed no edema.

On admission, the erythrocytes numbered 4,480,000; leukocytes, 13,000, with polymorphonuclear cells, 87 per cent., and the hemoglobin, 78 per cent.

Blood chemistry: The urea nitrogen was 36.0 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 70.0 mg.; uric acid nitrogen, 3.0 mg.; creatinin nitrogen, 2.2 mg. per hundred cubic centimeters of blood; cholesterin, 0.320 per cent., and sugar, 0.075 per cent.

Urinalysis: The reaction was acid; specific gravity, 1.016; albumin, a heavy trace, and no sugar. Microscopically, a few hyaline and granular casts, and an occasional red blood cell were seen.

Ophthalmologic examination (Dr. Wolff): The left disk was white and was raised by a dense exudate containing small, shiny white spots. This exudate tapered off gradually for a considerable distance into the retina, and at its uppermost edge broke off into clusters of small, round exudate. The center of the disk was elevated from three to four diopters. The retinal veins were full and tortuous, but no hemorrhages were present. The right disk showed the same condition, but in a less degree. The systolic blood pressure was 205.

Roentgen-ray measurements of the heart were as follows: left transverse diameter, 7.75 cm.; right transverse diameter, 2.5 cm.; oblique diameter, 10.5 cm.; arch, 4.5 cm. Roentgen-ray examination of the various arteries was negative.

From the physical examination and the laboratory findings, we may deduce marked hypertension, some cardiac hypertrophy, polyuria, albuminuric retinitis and retention of nitrogenous substances in the blood.

Course in Hospital.—The patient's entire stay in the hospital was thirteen days. The duration of the acute symptoms was about eight weeks, and the entire course of the disease perhaps not more than eight months. The general condition became gradually worse; the abdominal pain was almost continuous, and the stools contained fresh and old clotted blood. The blood pressure remained high—from 180 to 240 systolic, and from 130 to 180 diastolic. The phenolsulphonephthalein excretion was 30 per cent. in two hours. The character of the urine remained the same, and the output was regularly as great, if not greater, than the absolute fluid intake.

Purpuric spots appeared all over the child's body during the last week of her illness, yet the blood platelet count was 200,000. She became drowsy and appeared suburemic during the last few days of her life. A chemical examination of the blood taken a few days before death showed a urea nitrogren of 85.4 mg. per hundred cubic centimeters of blood; incoagulable nitrogen, 146.5 mg.; uric acid nitrogen, 6.9 mg., and creatinin nitrogen, 2.8 mg. per hundred cubic centimeters of blood.

Necropsy Findings.—The body was that of a markedly emaciated child of normal size. There was no postmortem discoloration, no icterus and no rigor mortis.

Heart: The weight was 240 gm. The left ventricle was enormous, and was hypertrophied. The anterior aspect of the pericardium showed a small milk spot. The heart muscle on section was normal in appearance. The tricuspids and pulmonary orifices were normal. The mitral orifice showed a slight, uniform thickening of both cusps, probably of an arteriosclerotic nature. The aortic cusp along its aortic aspect presented three dry, yellow patches of atheroma;

the posterior wall of the outflow track showed the distinct whitening of endocarditis. The aortic cusps showed a marked arteriosclerotic thickening of the corpora arantii. The arch of the aorta was of normal width and elasticity. At the root, just above the sinus of Valsalva, were a few small yellowish atheromatous markings in the intima, beginning in the descending part of the arch and extending throughout the thoracic and abdominal aorta. The iliac vessels showed numerous button-like thickenings of the media, over which the intima appeared to be normal. On section, the centers of these thickenings were usually found to contain some yellow atheromatous material. These nodules in the thoracic aorta surrounded the orifice of the intercostal vessels and markedly narrowed them. The largest nodes were about the size of a thumb nail. The systemic vessels throughout the body appeared to be uniformly thickened.

Lungs: Both lungs on section were found to be edematous, and scattered through both lower lobes were small areas of diffuse hemorrhages. The weight of the left lung was 180 gm.; of the right lung, 220 gm.

Thymus: This was normal.

Liver: This was larger than normal, weighing 875 gm. The surface was bluish brown, and there was intense passive congestion.

Gall-bladder and bile passages: These were normal.

Spleen: The weight was 70 gm., and it was normal in size. On section, the malphighian bodies were seen to be extremely prominent, and the pulp was dark red and apparently congested.

Kidneys: The right kidney was about the size of a large lima bean, and weighed 6 gm. The capsule was adherent to the organ. On section, the cortex appeared to be 1 mm. in width. Striation could not be made out. The organ cut firmly. The pelvis was reduced in size in proportion to the size of the kidney. The ureter was of normal width. The left kidney weighed about 150 gm. and was slightly larger than normal. The capsule stripped easily, leaving a smooth surface, dirty yellowish brown, with diffuse, darkened mottling and occasional pin-point hemorrhages. On section, the cortex was yellowish brown, with streaks of lighter yellow, apparently fatty. The cortical parenchyma was swollen so that the striations were obscured. The medulla was intensely congested. The pelvis and ureters were normal.

Bladder and pancreas: These were apparently normal.

The suprarenals: These were normal in size. On section, the cortex was found to be thinner than normal. It appeared as a thin, dry yellow line. The greater part of both suprarenals appeared to consist of a markedly hyperplastic medulla.

Gastro-intestinal tract: The stomach showed a few scattered hemorrhages. On the posterior wall, near the lesser curvature, were two shallow ulcers about 1 cm. in width. The intestines were moderately dilated. About 18 inches of the ileum, 12 inches from the ileocecal valve, was gangrenous and bound down into the pelvis by adhesions. The omentum was adherent to the mass of gangrenous intestine. There appeared to be no volvulus. The arteries and veins leading to the gangrenous area were apparently normal. The process was therefore due to an intussusception which was spontaneously reduced before death.

Diagnosis: Congenital hypoplasia of the right kidney was diagnosed, with subacute nephritis of the left kidney, presenile arteriosclerosis, cardiac hypertrophy, acute intussusception and gangrene of the ileum.

Microscopic Examination.—The left kidney showed typical glomerulotubular nephritis, which was fairly diffuse in extent. The process was subacute. Some of the glomeruli showed necrosis of some loops. In all the glomeruli was a swelling of the endothelium, an increase in nuclei and an almost complete obliteration of the outlines of the capillaries. Here and there, some of the glomeruli and other contiguous tubules were well preserved. The arteries and arterioles in the cortex showed marked thickening of their walls. The larger arteries were apparently not involved. In addition, there were areas in which the tubules were atrophic, and there was a marked increase in the interstitial connective tissue resembling replacement fibrosis. It is possible that some of these areas were examples of focal nephrosclerosis complicating diffuse nephritis. The right kidney showed a cortex—or what was left of it—consisting of a small amount of dense, purulent connective tissue in which were imbedded numerous glomeruli and strands of atrophic tubules. Only a few small islands of well preserved tubules were seen. The medullary portion of the section and also some of the cortical portion consisted of a dense connective tissue in which were imbedded atrophic tubules. There were numerous thick-walled arteries and arterioles, the latter showing an enormous hyaline thickening, especially of the intima, which markedly narrowed the lumen.

Spleen: There was marked hyaline thickening of the wall of the arteries and arterioles, and lymphoid hypoplasia.

Suprarenal: There was a marked increase in the medulla tissue. The section contained numerous thick-walled arteries.

Heart muscle: There was moderate hyaline thickening of both media and intima in many of the small arteries in the interstitial apaces.

Aorta: There was button-like thickening of the intima involving the adjacent portion of the media, consisting of a peculiar homogeneous matrix which stained greenish blue, looking almost like the matrix of myxomatous tissue. Scattered in it were spindle-shaped and star-shaped fibroblasts similar to those in myxomatous tissue. The media also showed streaks of degeneration scattered through it which took the same blue stain. This bluish material appeared to result from a peculiar degeneration of the entire elastic system in the media.

Arteries: The external iliac artery showed the same degeneration of the media as was seen in the aorta. The muscle fibers in the media were in places atrophic and were spread apart by a peculiar homogeneous bluish stain, apparently a degenerated part of the elastic substance. On one side of the vessel was a button-like thickening of the media, which consisted of the same myxomatous-like structure seen in the aorta. The lumen o fthe vessel was partially occluded by a mass of round cells and polymorphonuclear leukocytes imbedded in some fibers. The adventitia showed no changes that could be considered characteristic of syphilis. The common iliac arteries showed areas of degeneration in the media resembling those already described, but here they were more diffuse and more uniformly distributed within the circumference of the vessel.

Case 3.—A girl, aged 11½ years, whose mother, father, and five brothers and sisters were well, and who gave no history of familial disease of any sort, was a full-term child, of fair general health with poor appetite; always thin, and constipated. She had had pneumonia when 2 years of age, and was sick for ten weeks when 4 years old, the diagnosis being unknown. There had been no scarlet fever, diphtheria or pertussis. She had had nocturia during the past six months. There had been no epistaxis, fever or night sweats. The patient had had marked anemia for the last six or eight months.

The first symptoms of the present illness noted by the mother were swelling about the eyes and severe headaches. A urinalysis had been made for the first time about six weeks before admission to the hospital and had shown "kidney trouble." Four weeks before, the child had had a sudden attack of convulsions and coma lasting a few days, and another attack two weeks before. Slight edema of the legs had appeared a week previously. Anorexia was marked. Dyspnea, weakness and pallor were increasing.

Examination.—The child had a convulsion on admission to the hospital; her mind was dissociated, and she was in a semicomatose condition. Vision was so poor that she could scarcely recognize fingers at a distance. Nutrition was excellent. The skin was very pale, with slight puffiness about the face. The pupils reacted to light, and no abnormal reflexes were present. Teeth, tonsils and pharynx were in good condition. The lungs were normal on percussion and auscultation. The heart was enlarged to the left. The apex beat was in the sixth interspace. The second sound at the base and at the apex was accentuated, and there were no murmurs. The radial arteries were not felt, and the temporal arteries were not visible. The pulse was rapid and of high tension. The abdomen was normal to palpation and percussion. The liver and spleen were not palpable. The extremities showed slight pretibial edema.

Blood examination: The erythrocytes numbered 1,660,000; leukocytes, 25,000, with polymorphonuclear cells, 87 per cent., and hemoglobin, 19 per cent.

Blood chemistry: The incoagulable nitrogen was 78 mg. per hunderd cubic centimeters of blood; uric acid nitrogen, 5.2 mg.; creatinin nitrogen 3.8 mg. per hundred cubic centimeters of blood; sugar, 0.120 per cent., and carbon dioxid 48 per cent. by volume. The Wassermann reaction of the blood and spinal fluid was negative. There was 25.2 mg. of urea nitrogen, and 0.3 mg. of uric acid nitrogen per hundred cubic centimeters of spinal fluid. The blood pressure was 190 systolic and 140 diastolic.

Course.—On admission, Aug. 15, 1920, a phlebotomy was performed immediately.

August 16: The general condition was improved. The sensorium was clear. The blood pressure was 190. Phenolsulphonephthalein excretion was 5 per cent. in two hours, and the dye was still present in the urine eleven hours later.

August 18: There had been no convulsions since admission. The vision was improving.

TABLE 2.—*Chemical Examination of Blood Before and After Transfusion*

	Before Transfusion, Mg.*	Two Days After Transfusion, Mg.*
Incoagulable nitrogen	109.0	87.0
Urea nitrogen	60.0	56.0
Uric acid	5.6	6.0
Creatinin	4.0	5.0

* Per hundred cubic centimeters of blood.

Ophthalmologic examination (Dr. Wolff): The left disk showed tremendous papilledema. The swelling was at least five diopters. At the same time, the disk was very pale, probably because of the intense anemia. A large group of glistening white spots was situated at the outer side of the disk. There were no hemorrhages. The right fundus was similar to the left, except that the swelling was less.

Blood examination: Hemoglobin was 20 per cent.; the polymorphonuclear cells, 90 per cent., with lymphocytes, 10 per cent. The blood smear showed a moderate anisocytosis and poikilocytosis. A transfusion of 12 ounces (355 c.c.) of blood, with a previous withdrawal of 8 ounces (236 c.c.) was performed. The systolic blood pressure before the transfusion was 212, but after the withdrawal of the 8 ounces was 184. With the introduction of 200 c.c. of blood, the pressure rose to 192, and immediately after the completion of the transfusion (a total of 370 c.c. of blood), the blood pressure was 200. Table 2 shows the results of the chemical examination of the blood before and after transfusion.

The total quantity of urine the day before transfusion was 1,040 c.c., with an incoagulable nitrogen content of 0.14 gm., and a sodium chlorid content of 2.57 gm.

The water test of 500 c.c. gave the results shown in Table 3.

The total urine in the first four hours was 190 c.c.; total night urine, 560 c.c., and total twenty-four hour volume, 700 c.c.

This water test shows clearly that the total quantity excreted was greater than the amount ingested, even though the amount ingested was very small; that the amount in the first four hours did not by any means equal the intake, and that the night urine exceeded the intake, although the fluid ingested was given at 8 a. m. In addition, it was demonstrated that, with the low excretion in the first four hours there was a fixation of specific gravity, and, even with the nocturia, this fixation was still present.

August 19: Intravenous phenolsulphonephthalein administration revealed only 5 per cent. excretion of the dye in two hours. The hemoglobin was 23 per cent.

August 28: The child was doing comparatively well. The hemoglobin was 31 per cent.; the blood pressure was 178.

September 12: The child was comfortable, and out of bed and about the ward.

September 25: The patient was in fairly good condition. The hemoglobin was 45 per cent., and the blood pressure was 215. The child began to have general convulsions, which kept up for the entire day, and semicoma continued for a few days.

December 15: The child's general condition again improved. There had been no convulsions for two months. There was a hemoglobin of 40 per cent. The systolic blood pressure was about 200. The urine examination revealed traces of albumin, with occasional hyaline casts. The patient was discharged from the hospital against advice, but was observed in her home. She was readmitted, Feb. 21, 1921, two months later. During the interval, she had been free from convulsions, but she became weaker and more anemic. She died a few days after her readmission. Two days before death, a chemical examination of the blood showed urea nitrogen 61 mg. per hundred cubic centimeters of blood; uric acid nitrogen, 2.5 mg., and creatinin nitrogen, 4.2 mg.

Table 3.—*Water Test*

	Hour									
	8:30 a.m.	9:00 a.m.	9:30 a.m.	10:00 a.m.	10:30 a.m.	11:30 a.m.	Total	8:00 p.m.	6:00 a.m.	8:00 a.m.
Volume (c.c.)	70	25	20	15	25	35	190	170	240	150
Specific gravity	1.010	1.008	1.006	1.006	1.010	1.011		1.010	1.009	1.011

Necropsy was not permitted.

ETIOLOGY

From a study of the histories and the course of these cases, it is impossible to ascribe any one definite causative factor. One patient had had scarlet fever, but in the others there was no history of infectious diseases. Alcohol, tobacco or a metallic poison could be excluded.

In Case 1, the patient had the wrinkled, wizened appearance associated with renal infantilism, described so well by the English authors, Miller and Parsons[2] and others. The previous history was unsatisfactory and, since the child was only 3½ years of age, it was impossible to state how long his general condition had been below normal, and just what his growth impulse was during his short span of life. Careful abdominal examination seemed to exclude the presence of congenitally cystic kidneys, and the absence of marked nitrogen retention seemed to exclude a marked malformation of the kidney; for it has been our experience that surgical conditions of the kidney, such as infective hydronephroses and various congenital malformations give a much higher nitrogen retention, in the hundreds of milligrams of nitrogen per hundred cubic centimeters of blood, than do the ordinary medical diseases of the kidney.

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[2] Miller, L., and Parsons, L.: Brit. J. Child. Dis. **9,** July, 1912.

Necropsy in Case 2 disclosed that one kidney was practically absent, and that the other, although slightly larger than normal, was badly diseased. In spite of this, the growth and nutrition of the child were excellent. From this case and many others described in the literature of the subject, it can be seen that there is a congenital element in many of these cases, the remaining kidney or the deformed kidneys being insufficient to carry on the work properly; or perhaps, as Pepper and Lucke[3] have suggested, the one apparently normal kidney is especially prone to chronic inflammatory processes.

Case 3 presented the cardinal symptoms of this group, yet was essentially different in two important particulars. First, there was much less arterial thickening; secondly, there was a profound secondary anemia. Without a postmortem examination, it was impossible to say how much arteriosclerosis was present, but clinically it seemed to be much less than in the other two cases. A certain number of cases in this group, then, had an underlying congenital basis; others have a hereditary predisposition, as shown in the cases described by Brill and Libman.[4]

SYMPTOMS AND COURSE

All three cases were characterized by a rapid course, and, although the exact length of time cannot be definitely stated, all died within a year after the onset of any noticeable symptoms. Volhard[5] has described a bland, or slowly progressing, form of hypertension nephritis (contracted kidney or *Schrumpfniere*) and a malignant, rapidly progressing form. In the former, there is no kidney insufficiency nor are there cardiac symptoms, but a slowly increasing hypertension. From my experience and from the study of the literature, these cases must be very rare in infancy and childhood. The malignant form of the adult has much in common with the group we are describing. Yet, the underlying etiologic factors, such as congenital anomalies and hereditary influences, which appear in many cases to be a dominant feature of this condition in children, prevent us from describing this group as one of primary contracted kidney. It has therefore seemed best to us to group them as cases of malignant hypertension nephritis, with varying anatomic and heritary causes.

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[3] Pepper, O. H. P., and Lucke, Baldwin: Fatal Chronic Nephritis in a Fourteen Year Old Girl with Only One kidney and a History of Scarlet Fever, Arch. Int. Med. **27**:661 (June) 1921.

[4] Brill, N., and Libman, E.: J. Exper. Med. **4**:541, 1899.

[5] Volhard, F.: Die Doppelseitigen Hematogenen Nierenerkrankungen, Julius Springer, 1918.

The subjective symptoms seemed very vague until the kidney insufficiency was far advanced; for there was relatively little history of complaint, except perhaps of a general feeling of weakness and malaise. Headache and vomiting were not prominent features until the condition was well advanced. Most interesting and important, and present in all three cases, was the marked abdominal pain. This pain came on at about the same time that the urinary disturbances were noticed, but the pain was the chief complaint in all three cases. So pregnant was this symptom that, when the second and third cases were admitted to the hospital, blood pressure and eyeground examinations were immediately made, and the true condition was discovered. The exact cause of this pain could not be determined; yet it had a marked resemblance to the "abdominal angina" that adults with hypertension have. In Case 2, necropsy revealed an intussusception; yet this could not have been the cause of the pain of about four months' duration, for the intussusception seemed to be of recent origin. Drugs producing arterial dilatation had no effect on the pain.

The growth and nutrition of the second and third patients were all that could be desired. But it seemed that Case 1 might be placed in the category of renal infantilism. Unfortunately, we could not obtain a necropsy, so the type of lesion could not be determined.

The kidney function in all cases, as shown by an examination of the urine and of the blood, was profoundly disturbed. The urinary output was greater than the absolute fluid intake. There were polyuria and fixation of specific gravity at a low level, and a slight amount of albumin and a small number of hyaline and granular casts were present in the urine. A chemical examination of the blood for its nitrogenous constituents showed that, in one case, there was a very moderate increase of the nitrogenous elements in the blood. Case 2, however, showed marked retention of nitrogen, and as it proved, presented a congenital lesion. It is a temptation to deduce from this that our first case had no congenital deformity; yet we are loath to do so, for our experience is as yet too small.

The phenolsulphonephthalein output was only moderately diminished in Case 1, but in Case 3 it was almost nil, even when the drug was given intravenously.

The hypertension in these cases was marked and constant, both the systolic and diastolic pressures being greatly increased. This is hardly the place to go into a discussion as to the cause of the hypertension, whether primary or secondary to the kidney lesion, or whether due to an extrarenal poisoning affecting the capillaries of the body. The action of this poison must have been different in our last case, for the arterial thickening was absent and anemia was marked.

Clinical examination of the blood showed no anemia in the first and second cases, although there was marked nitrogen retention in the latter. So nitrogen retention alone cannot account for the severe anemia which was present in our third case. This would bear out the observations made by Brown and Roth [6] at the Mayo Clinic. According to Volhard, there is often a polycythemia in the primary contracted kidney, and an anemia in the secondarily contracted kidney.

The ophthalmologic findings were characteristic of these cases, and similar to those found in the last stages of hypertension nephritis in the adult. There was a marked albuminuric retinitis present in all cases, which, according to Volhard, is supposed to be due to the constantly high blood pressure and the consequent ischemic condition of the retina.

The heart in all our cases showed a moderate hypertrophy of the left ventricle. The blood vessels in the case that came to necropsy showed marked arteriosclerosis.

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[6] Brown, G. E., and Roth, Grace M.: Anemia of Chronic Nephritis, Arch. Int. Med. **30**:817 (Dec.) 1922.

STUDIES IN THE URIC ACID METABOLISM OF CHILDREN *

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There is, perhaps, no nitrogenous substance in the urine that has been more carefully studied than uric acid. The majority of the investigations concerning the uric acid content of the urine which have been carried out have dealt chiefly with adults. The present report is of a study of the uric acid metabolism in children.

It was believed for a long time that uric acid in mammalian urine was an intermediary product of protein metabolism which was almost completely oxidized by the body to urea. We now know that this point of view is fundamentally incorrect, and that uric acid is derived from the catabolism of the nucleins of both the food and the tissues. As is well known, the nucleins contain nucleic acid, which in turn contains purins. It is the oxidation of the purins that yields uric acid.

The variations in the total daily elimination of uric acid, following different diets, varying states of health and individual idiosyncrasies, have been determined by numerous investigators. The fact that purins are found in the urine during starvation and on a purin-free diet has led to considerable investigation, in a search for some source for purins within the organism, beside that of ingested nucleins. Burian and Schur,[1] who were the first to distinguish clearly between exogenous and endogenous uric acid, maintained that while the endogenous fraction of uric acid might show variation depending on individual differences, the amount eliminated by one individual remained fairly constant, and the quantity was not altered by the intake of purin-free food.

Other investigators, Siven,[2] Hall,[3] Brugsch and Schittenhelm,[4] have also emphasized the fact that the output of endogenous uric acid during the twenty-four hour period is constant for one person, but the fact that the endogenous uric acid is not altered by the intake of purin free

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* Received for publication, Dec. 7, 1923.

* From the Pathological Laboratory and the A. Jacobi Division for Children of the Lenox Hill Hospital.

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3. Hall, I. W.: The Purin Bodies of Foodstuffs, Manchester, Sherratt and Hughes, 1902.

4. Brugsch, T., and Schittenhelm, A.: Der Nukleinstoffwechsel und seine Storungen, Jena, G. Fischer, 1910.

food has not been accepted. Mares,[5] Taylor and Rose,[6] Hopkins and Hope,[7] Smetanka,[8] Lambling and Dubois,[9] Folin,[10] Mendel and Stehle,[11] have demonstrated that the ingestion of food free from purin precursors, particularly the proteins, may, in any person, markedly raise the level of endogenous uric acid excretion. Mares suggests that this may be the results of the wear and tear on the nuclear material of the secretory glands of the gastro-intestinal tract, brought about by the work of secretion occasioned by the presence of food in the alimentary tract; though Lewis [12] and his co-workers are not of this opinion. The latter investigators suggest that the effect may be due to a general stimulation of all cellular metabolism by amino-acids, products of protein metabolism, a theory which has been fully discussed by Rose,[13] who has given further evidence to support it. Hermann,[14] in studying the effect of adding to a normal mixed diet fat in the form of butter, noticed a diminished output of uric acid, but concluded that fat had no effect on uric acid elimination. Umeda [15] found that on a fat-rich, carbohydrate-poor diet the excretion of uric acid was diminished, but attributed the effect to the acidosis occasioned by the lack of carbohydrates. Horbaczewski and Kanera,[16] who added 100 gm. of fat to a high protein diet, observed a slight decrease in the uric acid elimination, which they attributed to a weak protein sparing action of the fats. Lewis and Corley [17] could not demonstrate any influence on the hourly elimination of uric acid in the fasting individual, after the administration of fat (cream) in amounts up to approximately 135 gm. Smetanka found an increased excretion of uric acid after the ingestion of large amounts of honey (from 200 to 300 gm.) and potatoes (from 375 to 450 gm.), an effect thought by them to be due to the increased activity of the liver cells in the formation of glycogen. Lewis and Corley found that lactose, sucrose and glucose in moderate amounts (100 gm.) did not influence uric acid elimination, though honey and commercial glucose syrup in amounts greater than 200 gm. caused increased elimination. This increase, however, was neither as constant nor as marked as that which followed the

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ingestion of amino-acids or glycerin. According to Höst,[18] an increase in caloric intake beyond a certain minimum increases the endogenous uric acid, and the greater increase is, in his opinion, due to the protein intake. Neuwirth,[19] who confirmed the results obtained by Mendel and Stehle, showed that within certain limits there was a relationship between urinary volume and uric acid excretion, and that as a rule a decrease in urinary output meant a decrease in uric acid elimination, and further that a marked fall in the uric acid output occurred during the morning hours, and was followed by a further gradual decline during the afternoon.

METABOLIC STUDIES

Our studies were made on five normal children, who were kept under careful observation in the hospital wards. The uric acid metabolism was investigated under varying conditions, the general plan of which is here briefly presented: There was, in all instances, a preliminary period during which a weighed mixed purin-free diet was administered. This was followed by a period, during which measured amounts of water and four bran muffins were allowed. In the third period, the diet was high in carbohydrates and low in fats, while in the fourth period it was rich in proteins and low in carbohydrates and fats. In the fifth period, the fat content was high and the protein and carbohydrate low. All these diets were purin-free. The duration of each period varied from two to four days and the order in which they were introduced differed in each case. This was done in order to determine whether the same results would be obtained regardless of the order in which the dietary periods were introduced. Each day, at approximately the same time, the patients were weighed, and on the second day of each period, at approximately the same time, chemical examinations of the blood (urea nitrogen, van Slyke and Cullen method; creatinin and sugar, Myers and Fine method; uric acid, Benedict[20] method) were made, with the patient in a fasting condition. The caloric value of each diet was noted; the fluid intake and output for each twenty-four hour period was determined, and the total uric acid elimination was estimated (Benedict[21] method). For one or two days of each period, a measured amount of uric acid was given by mouth, and for at least one day in each period the uric acid elimination in the urine was estimated at two hour intervals.

REPORT OF CASES

Case 1 (Tables 1, 2, 3).—H. S., aged 8 years, observed for a period of nineteen days, during the first four days was given a mixed purin-free diet

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consisting of protein, 80 gm.; fat, 94 gm.; carbohydrate, 54 gm. To this, on the second and third day, 1 gm. of uric acid was added, and blood chemistry determinations were made on the second day. A three-day period followed, during which the diet consisted of a measured amount of water and four bran muffins. On the second and third day of this period, 1 gm. of uric acid was given by mouth, and chemical examinations of the blood were made on the second day.

TABLE 1 *(Case 1).—Summary of Findings: Chronic Cervical Adenitis*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
9/21	Mixed, normal.........	80	94	54	1,424	24.5	1,200	1,100	260	None
9/22*	Normal................	80	94	54	1.424	24.5	1,200	1,180	277	1 gm.
9/23	Normal................	80	94	54	1,424	24.5	1,200	1,170	300	1 gm.
9/24	Normal................	80	94	54	1,424	24.2	1,200	1,035	325	None
9/25	Fasting................	0	0	0	0	23.9	1,000	900	228	None
9/26*	Fasting................	0	0	0	0	23.6	1,000	950	194	1 gm.
9/27	Fasting................	0	0	0	0	23.1	1,000	980	113	1 gm.
9/28	High carbohydrate....	19	7	303	1,385	23.1	1,100	1,020	260	None
9/29*	High carbohydrate....	19	7	303	1,385	23.3	1,200	1,130	265	1 gm.
9/30	High carbohydrate....	19	7	303	1,385	23.4	1,200	1,184	230	1 gm.
10/ 1	High carbohydrate....	19	7	303	1,385	23.7	1,200	1,030	242	None
10/ 2	High fat...............	9	150	11	1,477	23.6	1,100	1,048	119	1 gm.
10/ 3*	High fat...............	9	150	11	1,477	23.2	1,200	1,156	112	1 gm.
10/ 4	High fat...............	9	150	11	1,477	23.1	1,200	1,120	115	None
10/ 5	Normal................	80	94	54	1,424	23.4	1,200	1,110	247	None
10/ 6*	Normal................	80	94	54	1,424	23.6	1,200	1,140	273	1 gm.
10/ 7	High protein...........	148	13	68	1,007	23.7	1,600	1,540	358	None
10/ 8*	High protein...........	148	13	68	1,007	23.9	1,600	1,560	388	1 gm.
10/ 9	High protein...........	148	13	68	1.007	24.1	1,600	1,545	390	1 gm.

* Days on which blood chemistry determinations were made.

TABLE 2 *(Case 1).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
9/22............................	17.0	0.5	2.3	80
9/26............................	18.0	0.5	2.5	84
9/29............................	16.5	0.7	2.2	82
10/ 3............................	15.0	0.8	2.1	90
10/ 6............................	16.0	0.7	2.4	85
10/ 8............................	17.0	0.8	2.8	90

TABLE 3 *(Case 1).—Changes in Blood Chemistry Following Ingestion of Uric Acid During High Protein Period (Amount Given, 1 Gm., at 9 a. m.)*

		Time		Mg. per 100 C.c. Blood			
Date	Diet	A.M.	P.M.	Creatinin	Urea Nitrogen	Uric Acid	Sugar
10/9	High protein.......	9:30		0.8	17.0	2.9	80
		11:00		0.9	16.0	2.5	100
		12:00		—	15.0	3.0	—
			1:00	—	14.0	2.8	—
			2:00	—	14.5	2.7	—

For the next four days, a high carbohydrate diet was given, consisting of protein, 19 gm.; fat, 17 gm.; carbohydrate, 303 gm. The same uric acid feeding and chemical examinations of the blood were made as in the previous periods. Following this was a three-day period of a high fat diet consisting of protein, 9 gm.; fat, 150 gm.; carbohydrate, 11 gm.; 1 gm. of uric acid being given on the first and second days.

This period was followed by two days of a mixed purin-free diet similar to that of the first period, 1 gm. of uric acid being administered on the second day.

The diet of the last period was a high protein one consisting of protein, 148 gm.; fat, 13 gm.; carbohydrate, 68 gm., and again 1 gm. of uric acid was given on the second and third days. The blood chemistry determinations were made on the second day. The data of the various determinations are shown in Table 2.

On the last day of the above-mentioned period, 1 gm. of uric acid was given at 9 a. m. Chemical examinations of the blood were made at 9:30, 11 and 12 a. m., and at 1 and 2 p. m., to ascertain whether any changes occurred in the blood following the ingestion of uric acid. These results are given in Table 3.

Case 2 (Tables 4, 5, 6).—A. T., aged 10 years, was observed over a period of sixteen days. The arrangement of the various dietary periods is noted in Table 4, and is similar to that of Case 1, except for the order in which the

Table 4 *(Case 2).—Summary of Findings: Chorea*

									Uric Acid	
Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Excretion, Mg.	Uric Acid Feeding
10/16	Mixed	65	80	60	1,257	23.2	800	760	268	None
10/17*	Normal	65	80	60	1,257	23.3	900	820	234	1 gm.
10/18	Starvation	0	0	0	0	23.0	980	900	190	None
10/19*	Starvation	0	0	0	0	23.0	985	900	125	1 gm.
10/20*‡	Normal	80	90	75	1,473	23.4	1,000	940	243	None
10/21‡	Normal	80	90	75	1,473	23.6	1,100	1,080	229	1 gm.
10/22	High fat	8	200	10	2,188	23.2	900	850	195	None
10/23*	High fat	8	200	10	2,188	23.0	1,000	975	180	1 gm.
10/24	High fat	8	200	10	2,188	23.0	1,000	980	175	1 gm.
10/25	High carbohydrate	15	8	280	1,284	23.1	1,000	985	205	None
10/26*	High carbohydrate	15	8	280	1,284	23.1	1,000	985	234	1 gm.
10/27	High carbohydrate	15	8	280	1,284	23.3	1,000	995	230	1 gm.
10/28	High protein	250	12	7	1,155	23.3	1,000	990	265	None
10/29	High protein	250	12	7	1,155	23.4	1,000	994	273	1 gm.
10/30*	High protein	250	12	7	1,155	23.5	1,000	986	295	1 gm.
10/31	Normal	80	90	75	1,473	23.5	1,000	990	247	None

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

Table 5 *(Case 2).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/17	14.3	1.7	2.5	94
10/19	15.2	1.5	2.4	91
10/20	14.4	1.6	2.3	93
10/23	12.8	1.6	2.4	98
10/26	12.9	1.7	2.3	96
10/30	12.8	1.8	2.6	91

Table 6 *(Case 2).—Two Hourly Excretion of Uric Acid*

	Diet			Time		
Date	Protein	Fat	Carbohydrate	A.M. P.M.	Urine Output, C.c.	Uric Acid Excretion, Mg.
10/20	80	90	75	10:30–12:30	240	60.0
				2:30	165	33.5
				4:30	50	27.3
				6:30	90	19.2
				8:30	110	30.1
				P.M. A.M. 8:30–10:30	285	71.3
10/21	80	90	75	A.M. P.M. 10:30–12:30	235	45.3
				2:30	130	22.5
				4:30	75	20.0
				6:30	80	10.0
				8:30	110	25.7
				P.M. A.M. 8:30–10.30	450	105.0

periods were introduced. The two hourly excretion of uric acid was determined here for two successive days, October 20 and 21 (Table 6), the diet being a mixed purin-free one consisting of protein, 80 gm.; fat, 90 gm.; carbohydrate, 75 gm. On the second day (October 21), 1 gm. of uric acid was given. Specimens of urine were collected every two hours from 10:30 a. m. to 8:30 p. m., October 20, and one specimen from then until 10:30 a. m., October 21. The urine for the second day was similarly collected.

Case 3 (Tables 7, 8, 9, 10).—D. D., aged 9 years, observed over a period of nineteen days, was given a mixed purin-free diet, October 31, with 1 gm. of uric acid at 9 a. m. Chemical examinations of the blood were made at 9:30, 11 and 12 a. m., and at 1 and 2 p. m. (Table 10).

Table 7 *(Case 3).—Summary of Findings: Chorea*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/30	Mixed, normal.........	70	81	45	1,225	22.4	875	856	285	None
10/31*	Normal................	70	81	45	1,225	22.3	900	890	261	1 gm.
11/1	Normal................	70	81	45	1,225	22.3	900	880	264	1 gm.
11/2‡	Normal................	70	81	45	1,225	22.5	1,200	1,124	268	None
11/3	Normal................	70	81	45	1,225	22.4	1,000	980	235	None
11/4	Starvation............	0	0	0	0	22.1	1,000	985	121	None
11/5*	Starvation............	0	0	0	0	22.0	1,000	987	101	1 gm.
11/6	Starvation............	0	0	0	0	21.8	1,000	970	100	1 gm.
11/7	High fat..............	12	110	15	1,134	21.9	1,000	986	164	None
11/8*	High fat..............	12	110	15	1,134	22.1	1,000	990	167	1 gm.
11/9	High fat..............	12	110	15	1,134	22.1	1,000	982	182	1 gm.
11/10	High protein..........	220	30	20	1,263	22.3	1,000	974	224	None
11/11*	High protein..........	220	30	20	1,263	22.5	1,000	990	287	1 gm.
11/12	High protein..........	220	30	20	1,263	22.7	1,000	960	305	1 gm.
11/13	Starvation............	0	0	0	0	22.5	1,000	870	147	None
11/14*‡	Starvation............	0	0	0	0	22.3	1,200	1,124	127.3	1 gm.
11/15	High carbohydrate....	20	12	300	1,424	22.4	1,000	988	167	None
11/16*	High carbohydrate....	20	12	300	1.424	22.6	1,000	970	210	1 gm.
11/17	High carbohydrate....	20	12	300	1,424	22.8	1,000	910	250	None

* Days on which blood chemistry determinations were made
‡ Collection of urine in two hourly periods during the day.

Table 8 *(Case 3).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/31...........................	15.0	1.8	3.1	108
11/5...........................	14.0	1.6	2.8	98
11/8...........................	15.0	1.6	2.7	96
11/11...........................	14.0	1.5	2.6	98
11/14...........................	14.3	1.2	2.3	104
11/16...........................	15.0	1.5	2.8	94

Table 9 *(Case 3).—Two Hourly Excretion of Uric Acid*

Date	Diet			Time	Urine Output, C.c.	Uric Acid Excretion, Mg.
	Protein	Fat	Carbohydrate	A.M. P.M.		
11/2...............	70	81	45	10:30-12:30	310	53.0
				2:30	137	30.5
				4:30	125	28.0
				6.30	48	12.0
				8:30	154	37.0
				P.M. A.M.		
				8:30-10:30	350	107.5
				A.M. P.M.		
11/14...............	0	0	0	10:30-12:30	260	24.2
				2:30	180	19.0
				4:30	110	18.1
				6:30	90	14.0
				8:30	174	22.0
				P M. A.M.		
				8:30-10:30	310	30.0

Table 10 *(Case 3).—Changes in Blood Chemistry Following Ingestion of Uric Acid, During Mixed Purin-Free Diet (Amount Given, 1 Gm., at 9 p. m.)*

		Time		Mg. per 100 C.c. Blood			
Date	Diet	A.M.	P.M.	Creatinin	Urea Nitrogen	Uric Acid	Sugar
10/31	Mixed..............	9:30		1.8	15.0	3.1	108
		11:30		1.5	16.5	2.8	96
		12:00		—	16.0	3.3	—
			1:00	—	14.0	3.0	—
			2:00	—	14.0	2.9	—

Case 4 (Tables 11, 12, 13).—B. C., aged 7 years, was observed for six days.

Table 11 *(Case 4).—Summary of Findings: Convalescent from Pneumonia*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/16	Mixed..................	65	80	60	1,257	25.5	1,300	1,290	336.5	None
10/17*	Normal................	65	80	60	1,257	25.3	1,300	1,200	313	1 gm.
10/18	Starvation............	0	0	0	0	25.1	1,000	970	200	None
10/19*	Starvation............	0	0	0	0	24.9	1,000	980	140	1 gm.
10/20‡	Normal................	80	90	75	1,473	24.8	960	838	237	None
10/21*‡	Normal................	80	90	75	1,473	24.9	1,100	1,022	228	1 gm.

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

Table 12 *(Case 4).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/17............................	16.5	0.5	3.0	82
10/19............................	15.0	0.7	3.2	90
10/21............................	18.0	0.6	3.0	84

Table 13 *(Case 4).—Two Hourly Excretion of Uric Acid*

	Diet			Time		
Date	Protein	Fat	Carbohydrate	A.M. P.M.	Urine Output, C.c.	Uric Acid Excretion Mg.
10/20..............	80	90	75	10:30–12:30	239	59.8
				2:30*	90	28.4
				4:30	52	26.0
				6:30	31	18.0
				8:30	170	32.0
				P.M. A.M.		
				8:30–10:30	256	73.0
				A.M. P.M.		
10/21..............	80	90	75	10:30–12:30	255	30.6
				2:30	106	24.5
				4:30	91	21.0
				6:30	61	18.3
				8:30	79	27.0
				P.M. A.M.		
				8:30–10:30	430	107.5

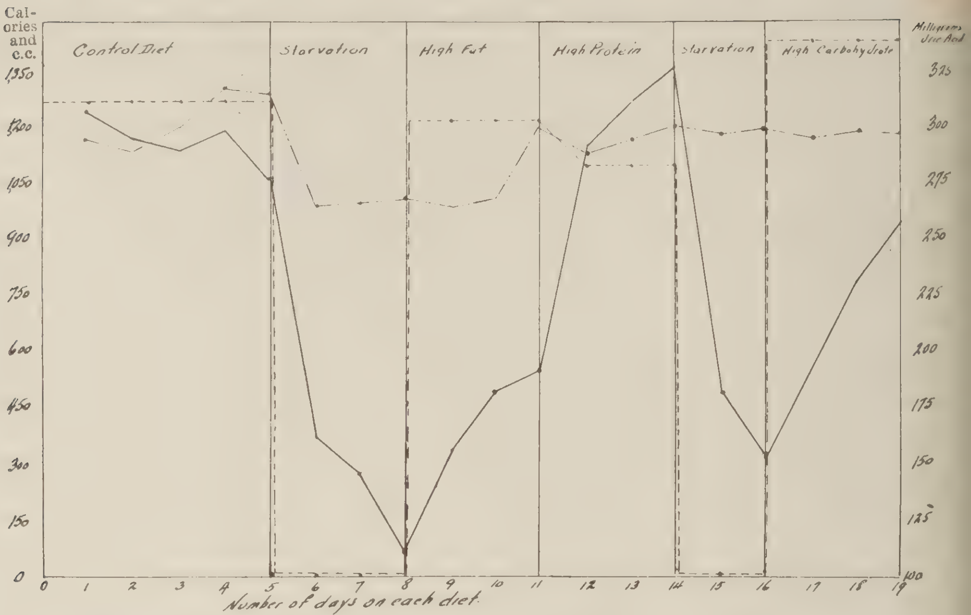

Chart 1 (Case 5).—Relationship between (*a*) uric acid excretion and caloric intake; (*b*) uric acid excretion and water output; straight line, uric acid excretion; broken line, caloric intake; dot and dash line, water output.

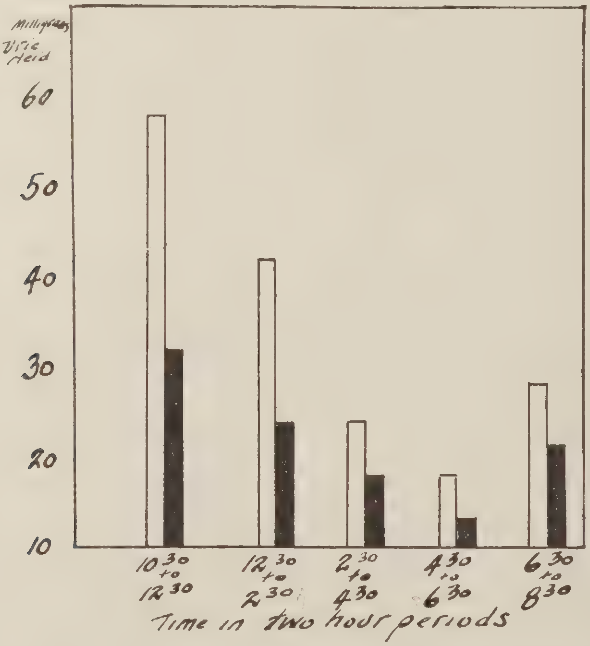

Chart 2 (Case 5).—Two hour periods of uric acid excretion on control diet and starvation; control, white; starvation, black.

CASE 5 (Tables 14, 15, 16).—A. W., aged 12 years, was studied for nineteen days. The procedure was similar to that in the other cases.

TABLE 14 *(Case 5).—Summary of Findings: Chorea*

Date	Diet	Protein	Fat	Carbohydrate	Calories	Body Weight, Kg.	Intake, C.c.	Output, C.c.	Uric Acid Excretion, Mg.	Uric Acid Feeding
10/30	Mixed, normal.........	90	70	60	1,260	33.2	1,200	1,160	305	None
10/31*	Mixed..................	90	70	60	1,260	33.2	1,200	1,120	294	1 gm.
11/ 1	Mixed..................	90	70	60	1,260	33.1	1,280	1,190	288	None
11/ 2‡	Mixed..................	90	70	60	1,260	33.0	1,300	1,293	296	None
11/ 3	Mixed..................	90	70	60	1,260	33.1	1,300	1,285	275	None
11/ 4	Starvation............	0	0	0	0	32.9	1,000	985	160	None
11/ 5*	Starvation............	0	0	0	0	32.7	1,000	990	145	1 gm.
11/ 6	Starvation............	0	0	0	0	32.6	1,000	994	110	None
11/ 7	High fat...............	10	120	12	1,206	32.5	1,000	984	155	None
11/ 8*	High fat...............	10	120	12	1,206	32.2	1,000	992	180	1 gm.
11/ 9	High fat...............	10	120	12	1,206	32.2	1,200	1,180	190	None
11/10	High protein...........	200	15	30	1,083	32.3	1,200	1,120	290	None
11/11*	High protein...........	200	15	30	1,083	32.5	1,200	1,165	310	1 gm.
11/12	High protein...........	200	15	30	1,083	32.5	1,200	1,180	325	None
11/13	Starvation............	0	0	0	0	32.4	1,200	1,170	180	None
11/14*‡	Starvation............	0	0	0	0	32.4	1,200	920	152	1 gm.
11/15	High carbohydrate....	15	10	320	1,467	32.5	1,200	1,160	190	None
11/16*	High carbohydrate....	15	10	320	1,467	32.7	1,200	1,175	230	1 gm.
11/17	High carbohydrate....	15	10	320	1,467	32.9	1,200	1,170	255	None

* Days on which blood chemistry determinations were made.
‡ Collection of urine in two hourly periods during the day.

TABLE 15 *(Case 5).—Blood Chemistry Determinations*

Date	Urea Nitrogen, Mg. per 100 C.c.	Creatinin, Mg. per 100 C.c.	Uric Acid, Mg. per 100 C.c.	Sugar, Mg. per 100 C.c.
10/31..........................	14.8	1.4	2.5	102
11/ 5..........................	13.4	1.8	2.1	108
11/ 8..........................	12.5	1.6	2.1	96
11/11..........................	15.2	1.8	2.7	98
11/14..........................	14.7	1.6	2.5	96
11/16..........................	14.8	1.5	2.3	94

TABLE 16 *(Case 5).—Hourly Excretion of Uric Acid*

	Diet			Time	Urine Output,	Uric Acid Excretion,
Date	Protein	Fat	Carbohydrate	A.M. P.M.	C.c.	Mg.
11/2...............	90	70	60	10:30–12:30	350	58
				2:30	248	42
				4:30	110	24
				6:30	70	20
				8:30	95	28
				P.M. A.M.		
				8:30–10:30	424	124
				A.M. P.M.		
11/14..............	0	0	0	10:30–12:30	230	32
				2:30	140	24
				4:30	115	18
				6:30	65	13
				8:30	70	21
				P.M. A.M.		
				8:30–10:30	300	44

BLOOD CHANGES IN THE URIC ACID METABOLISM

Tables 2, 5, 8, 12 and 15 show the results of chemical blood examinations made while the patients were kept on the different dietary regimens outlined at the beginning of the paper. A study of these tables reveals that the variations in the different blood constituents were very slight, particularly for the uric acid, and for all practical purposes may be disregarded.

When uric acid was fed and blood determinations were made at repeated intervals thereafter, only slight changes in the uric acid content of the blood were noted, in the two cases in which such examinations were made (Case 1, Table 3, and Case 3, Table 10). In Case 1, a high protein diet was allowed. At 9 a. m., 1 gm. of uric acid was fed to the patient and chemical examinations of the blood were made at 9:30, 11, 12 a. m. and also at 1 and 2 p. m. The blood uric acid at these intervals was 2.9, 2.5, 3.0, 2.8 and 2.7 mg., respectively. In Case 3, a mixed purin-free diet was allowed, while the rest of the procedure was the same as in Case 1. The blood uric acid at these intervals was 3.1, 2.8, 3.3, 3.0 and 2.9 mg. Whether these slight variations are of any significance is doubtful.

EFFECT OF DIFFERENT PURIN-FREE DIETS ON THE DAILY URIC ACID OUTPUT

As the results obtained were practically identical in the cases studied, one of the group will serve for the purposes of specific discussion. The data in each case may be obtained by reference to Tables 1, 4, 7, 11 and 14. Table 4 shows that on a mixed purin-free diet, the uric acid excretion for the twenty-four hour period was 268 mg. the first day and 234 mg. the second. This dietary period was considered the control period in our cases.

On the starvation diet the uric acid excretion fell to 190 mg. the first day and to 125 mg. the second. When the control diet was resumed, the twenty-four hour excretion rose to 243 mg., and on the following day was 229 mg. These figures are of interest because they show an increase in the uric acid excretion after the administration of food free from purins.

On a high fat diet, the uric acid excretion was considerably lower than that obtained on the mixed purin-free diet, and but slightly greater than that observed during the starvation period. In Case 2, the twenty-four hour excretion on the three successive days of the high fat diet dropped to 195, 180 and 175 mg. It will be noted that the sudden fall is similar to that observed during the starvation period. Evidently, the high fat diet has an inhibiting effect on the excretion of uric acid. This observation agrees with the results obtained by Hermann and Horbaczewski and Kanrera, but does not support the claims of Lewis and Corley.

While the caloric value of the high fat diet employed in Case 2 is higher than that of the other diets, its effect on uric acid excretion is almost the same as that of starvation. This is of interest since Höst found that an increase in the caloric intake beyond a certain minimum gave rise to an increase in the endogenous uric acid. The curve of excretion and its relation to caloric intake can be more readily comprehended by references to Chart 1, in which the numerical data in Case 5 are graphically shown.

During the three days of the high carbohydrate diet employed in Case 2, the uric acid excretion was 205, 234, and 230 mg. These results are almost the same as those obtained during the mixed purin-free diet period. In other cases, the excretion of uric acid was even less than that observed with the control diet. These results seem to be in opposition to those of Smetanka, who found that the uric acid excretion was increased after the administration of carbohydrates. However, they confirm the work of Lewis and Corley.

In all of the cases studied, a sharp rise in the uric acid output was noted immediately on the intake of a high protein diet, which was higher than that obtained on a mixed purin-free diet. In Case 2, the values were 265, 273 and 295 mg., respectively, for the three days. These results seem to be in accord with those obtained by other investigators, who have demonstrated that high protein diets raise the level of endogenous uric acid excretion, probably as the result of the catabolism of the nucleoproteins of the body tissues, which, as has been suggested by Lewis, may in part be aided by cellular metabolic stimulation from the amino-acids derived from the proteins. While a high protein diet is a factor in the increased elimination of uric acid, it cannot be regarded as a quantitative one, for the protein ingestion in Case 2 was almost four times as much as that of the control diet; whereas, the uric acid excretion was only about one-tenth greater than that observed with the control diet. A possible explanation may be that a slight increase of protein is sufficient to stimulate the organism to increased purin metabolism, and that further addition of protein increases the amount of uric acid elimination up to a point which may be termed the limit of protein action. Beyond this, an additional intake of protein is without appreciable effect on the uric acid elimination.

VARIATIONS IN THE URIC ACID ELIMINATION THROUGHOUT THE TWENTY-FOUR HOUR PERIOD

This phase of the problem was investigated in Cases 2, 3, 4 and 5, the results being recorded in Tables 6, 9, 13 and 16. In Cases 2 and 4, the two hourly excretion of uric acid was determined on two separate days, on a mixed purin-free diet. Cases 3 and 5, the examinations were made during the administration of a mixed purin-free diet and during a starvation period.

Table 6 shows the excretion to be highest between 10 and 12 in the morning, followed by a progressive fall until the minimum is reached at 6:30 in the evening, with a rise again at the 8 p. m. period. Neuwirth has reported similar findings, although he did not call particular attention to this fact. That the urinary volume has any bearing on this curve of elimination cannot be determined from the findings in our cases, although Neuwirth found that a decrease in water output was generally followed by a decrease in uric acid excretion. Our results do not confirm this statement. It will be noted that the output on the first day at 4:30 in the afternoon was 50 c c. and the uric acid excretion 27.3 mg., while at 6:30 p. m., the volume was 90 c c. and the uric acid only 19.2 mg. A more complete idea of the relation between urinary volume and uric acid excretion may be obtained by reference to Chart 1.

Why the uric acid excretion should be higher at 10:30 a. m. than at any other time of the day cannot be entirely explained by the increased urinary output; nor can it be attributed to the fact that this high period occurs after feeding, as the greatest decrease is observed directly after the evening meal, which was given at 5:30 p. m. We do not offer any explanation for this peculiar phenomenon of increased morning uric acid elimination.

SUMMARY

1. The uric acid elimination for the twenty-four hour period remained fairly constant for the same person, while on a mixed purin-free diet.

2. During the fasting condition, the uric acid elimination for the twenty-four hour period reaches a minimum, and averages approximately one third of the amount eliminated on a mixed purin-free diet.

3. A high protein diet results in a greater uric acid elimination than does a purin-free diet.

4. A diet high in carbohydrates does not result in a greater uric acid elimination, beyond that observed after a mixed purin-free diet.

5. A high fat diet produces a marked diminution in the uric acid elimination when compared with the amount eliminated on a mixed purin-free diet, and this amount is slightly higher than that eliminated during the fasting condition.

6. A study of the two hourly excretion of uric acid shows a high morning elimination, with a gradual decrease throughout the day, reaching a minimum late in the afternoon, with a slight secondary rise in the evening.

7. There is no relationship between the amount of uric acid eliminated and the total urinary output.

8. The uric acid elimination does not bear any relationship to the total caloric value of diet.

9. The feeding of uric acid does not influence the amount of uric acid eliminated in the urine.

10. The administration of uric acid does not influence the concentration of uric acid in the blood.

11. The blood concentrations of urea nitrogen, uric acid, creatinin and sugar remain unchanged regardless of the type of diet.

MEASLES TRANSMITTED BY BLOOD TRANSFUSION *

REPORT OF A CASE

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Much experimental work has been done on the transmission of infectious disease and the results are generally accepted. Experimental work, as a rule, is done on animals, and we assume that man reacts in a similar manner. Since infectious disease of man is common, we are interested to know how long the infection may be in his body before physical signs are present.

The transmission of measles has been studied for many years and clinical observation of cases has given much information. Because such observations could not explain certain details, Home of Edinburgh, in 1758, was prompted to attempt to produce measles experimentally, and since then many workers have attempted to produce this disease in various ways.

Hektoen[1] has reviewed the literature on transmission of measles to January, 1905. He collected blood early in measles, cultured it on ascites broth and then injected 4 c.c. under the skin of a healthy person. On the thirteenth day after injection, the temperature rose to 101 F.; on the fourteenth day, it rose to 103 F., and on the fifteenth day, the rash of measles appeared.

In a second case, he injected 5 c.c. of a mixture of blood in ascites broth subcutaneously into a healthy person. On the eleventh day, the temperature rose. On the thirteenth day, there was some cough. During the fourteenth night, the eruption of measles developed.

Anderson and Goldberger[2] inoculated monkeys intracerebrally and intraperitoneally with blood from human patients with measles; and on the eleventh day after the injection, there was a rise of temperature, but there was no rash.

These investigators[3] filtered blood from patients with measles and injected the filtrate into monkeys. On the tenth day after inoculation, there was a rise in temperature, and on the fifteenth day, measles developed.

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* Received for publication, Dec. 7, 1923.

[1] Hektoen, Ludvig: Experimental Measles, J. Infect. Dis. **2**:238-255, 1905.

[2] Anderson, J. F., and Goldberger, Joseph: The Period of Infectivity of Blood in Measles, J. A. M. A. **57**:113 (Sept. 11) 1911.

[3] Anderson, J. F., and Goldberger, Joseph: The Nature of the Virus of Measles, J. A. M. A. **57**:974 (Sept. 16) 1911.

Tunnicliff[4] cultivated a micrococcus from the blood of fifty patients in the preeruptive stages of measles.

Blake[5] inoculated monkeys with nasopharyngeal washings, and after from six to ten days, symptoms of measles developed.

Tunnicliff and Moody[6] gave a series of monkeys, guinea-pigs and rabbits intratracheal injections of washings from the nose and throats of patients with measles in the early stage, and obtained mild reactions.

A careful search of the literature does not reveal a case in which the blood from a patient having measles was injected into the blood stream of another person and produced measles. The following cases are of interest because it appears that measles did occur as a result of transfusion of blood, and an opportunity was presented to observe two cases in which measles was transmitted from the mother to the infant. Both cases were on the service of Dr. E. J. Huenekens in the pediatric service of the Minneapolis General Hospital.

REPCRT OF CASES

Case 1.—Baby H., girl, aged 9 months, was admitted to the hospital, March 21, 1923, because of swollen glands, otitis media, fever and loss of weight. Her condition did not improve under treatment, and as she could not retain her feedings and was steadily losing weight, a transfusion of blood was decided on. Groupings were made, and as it was found that she and her mother were in Group II, the mother was chosen as the donor. The mother appeared to be in good health.

April 4, 1923, in the morning the baby was given a sinus transfusion of 75 c.c. of citrated blood. The red blood cells, April 2, numbered 3,500,000; the lymphocytes, 11,800. After the transfusion, the red blood cells numbered 4,620,000; the leukocytes, 27,500; which can be explained as a reaction following the transfusion. In a few days, the number of leukocytes fell to 7,500, remaining at that level during the remainder of the patient's stay in the hospital. Two days after the transfusion, she was much improved and was able to retain her feedings. The temperature fell to 99.4 F., and remained at that level until April 12, when it rose to 102 F. (by rectum). The fever continued high and, April 17, a rash developed. Koplik spots were present, and a diagnosis of measles was made. The patient was then transferred to the contagious disease service. Bronchopneumonia developed, and she died, April 27.

In seeking an explanation as to why the patient had measles, we learned that, two days after the transfusion, the mother developed the disease. There were no cases of measles at our station. Only relatives of babies were permitted to come into the ward, and they always wore sterile gowns and were not permitted to approach or touch babies not their own, and were not allowed to take their own babies out of the cribs. On the morning the transfusion was given, the mother did not touch or come near the baby. Her last previous visit was made four days before the day of transfusion. The interval between admission and transfusion was fourteen days. The interval between the transfusion and the appearance of the rash in the baby was thirteen days. The interval between the transfusion and the development of measles in the mother was two days. The interval between the last visit of the mother and the time she developed measles was six days.

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[4] Tunnicliff, Ruth: The Cultivation of a Micrococcus from Blood in Preeruptive and Eruptive Stages of Measles, J. A. M. A. **68**:1028 (April 7) 1917.

[5] Blake, F. G.: Measles, Arch. Ped. **38**:90 (Feb.) 1921.

[6] Tunnicliff, Ruth, and Moody, W. B.: Experimental Measles by Inoculation of Monkeys, Guinea-Pigs and Rabbits with Green Producing Diplococcus, J. Infect. Dis. **31**:382 (Oct.) 1922.

It is unusual for babies of this age to have measles. Since there appears to have been no other source of infection, we are justified in concluding that measles was transmitted from the mother to the child through the transfused blood.

Case 2.—Baby V., girl, born Feb. 21, 1923, weight 2,225 gm., was fed by tube. She was sent home March 3, 1923, still fed by tube and weighing 2,200 gm. She was readmitted to the hospital, May 17, because of loss of weight and regurgitation. The family history was negative. The patient was an only child. She was nursed for two weeks only, and then, because of a breast abscess, modified cow's milk was given. She had regurgitated ever since leaving the hospital. Vomiting occurred soon after each feeding and occasionally was projectile in character. The patient, now 3 months of age, was a poorly nourished underdeveloped child. The skin turgor was very poor. Since she did not respond to treatment and continued to vomit and lose weight, it was decided to perform a transfusion. Groupings were made, and it was found that the baby was in Group II and the mother in Group IV. The mother appeared to be in good health, and as there were no signs of disease, she was chosen as the donor.

May 28, the baby was given 60 c.c. of citrated blood through the sinus, at 9 : 30 a. m.

Before the transfusion was complete, it was observed that she was not doing well. There was a convergent strabismus and some spasticity. She was put to bed and at 11 : 30 a. m. all symptoms were improved. She took her feedings well during the rest of the day. The rectal temperature was 99 F. The next day, the temperature was 101 F., and was at a normal level until June 10, when it rose to 100 F. Her condition was very good until June 5, when stools became diarrheal in character. This continued June 7 and 8, the stools being normal, June 9.

Nothing of note occurred until June 10, when the temperature rose to 100 F. The next day, the temperature was 101.6 F., and a rash developed. Koplik spots were present, and a diagnosis of measles was made. The patient was transferred to the contagious disease service. The measles ran the usual course, and the baby was returned to our station. The subsequent history was without events, and she was discharged from the hospital in a satisfactory condition, June 29. The laboratory findings during her stay were negative.

Again we sought for a cause of the measles. There were no cases of measles in our station. The patient had been in our station twenty-five days before developing measles. She occupied a crib in a remote corner of the ward. It was evident that she was infected with measles while in our station. The mother made no comment on the child having measles. On questioning, she denied that she had been sick, but later admitted that two days after the transfusion she developed measles and was sick for a week.

Here the interval between admission and transfusion was twenty-five days. The interval between transfusion and measles in the baby was fourteen days. The interval between the transfusion and development of the measles in the mother was two days.

The mother did not come in contact with the baby on the day of transfusion. She had visited it the day before, but did not handle it. The interval between the mother's last visit to the baby and her own illness was three days.

CONCLUSIONS

1. The virus of measles is present in the blood at least two days before the appearance of the rash.
2. Measles may be transmitted through the transfusion of blood.
3. The two cases seem to establish the incubation period at thirteen and fourteen days.
4. It would seem advisable to take a careful history of those who are to be donors for babies and to look for Koplik spots.

RECENT WORK IN ANATOMY, PHYSIOLOGY AND PATHOLOGY OF INFANCY AND CHILDHOOD *

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INFANT MORTALITY

As a result of his studies of infant mortality as shown by church registration in Schleswig-Holstein, Hanssen,[1] in Kiel, shows that in some places infant mortality was formerly lower than it is today. Eichede, with a present population of 2,900, had an infant mortality of 12 per cent. (twelve babies out of every hundred dying during the first year of life) during the period 1677-1722, as against a mortality of 14.5 per cent. for the period 1900-1912. Low rates are commonly ascribed to the wide use of breast-feeding, and the high rates to epidemics, chiefly of smallpox. It is noteworthy that apparently in former centuries the "summer peak" of infant mortality was not in evidence.

It would seem that the factors of rural population and northern climate might enter into these findings, but the overwhelming importance of breast-feeding in a rural population is shown in another study, on present-day conditions in the Austrian Tyrol,[2] among peasants who for many years have enjoyed excellent incomes and have hoarded treasures. Whereas, in Vienna, 9.9 per cent. of all children born in 1920 died within their first year of life, in two typically conservative and old-fashioned provinces with nine tenths of the population peasants, the figures ranged from 20 to 27 per cent. In some villages, a mortality of from 40 to 50 per cent. was found, and in the richest rural district of Austria, with a population of 767,000, the average was 27.6 per cent. (One child was born dead for each thirty-nine born alive.)

The main reason for this excessive death rate among infants was found in the custom of artificial feeding. This is practiced from lack of knowledge of the importance of breast-feeding, and because of immemorial custom, and carried on without knowledge of the simplest hygienic principles.

For America (registration area of the United States, population 70,000,000), the published birth and infant mortality rates show a birth rate of 24.3 per thousand population (a low record death rate of 11.7 per thousand), and a record low infant mortality rate (death during the first year of life) of 76 per thousand or 7.6 per cent. The corresponding figures for the preceding years were 23.7, 13.1, and 86, respectively—

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* Received for publication, Dec. 7, 1923.

[1] Berlin Letter, J. A. M. A. **80**:1396 (May) 1923.

[2] Vienna Letter, J. A. M. A. **80**:569 (Feb.) 1923.

8.6 per cent. Of the states, Oregon showed an infant mortality rate of 5.1 per cent. and Delaware, 9.8 per cent., and of the cities of 100,000 population or more, Portland, Ore., 5.0, and Fall River, 11.4 per cent.[3]

The death rate of mothers from childbirth in the birth registration area (nine states and the District of Columbia) for 1921, as compiled by the Bureau of the Census,[4] was 6.5 to each thousand live births. Previous rates were: 1915, 6.1; 1916, 6.2; 1917, 6.3; 1918, 1919, and 1920, high, owing presumably to the prevailing influenza which took a heavy toll of pregnant women. The ratio of death from childbirth to the number of women bearing children was about 1 to 150.

The lowest death rate, in this territory, from causes due to childbirth was 5.3 for each 1,000 live births (Connecticut), and the highest, 9.8 (South Carolina). The highest rate for white mothers was 7.8 (South Carolina), and for colored mothers, 14.8 (Kentucky).

The 1921 maternal death rate, 6.5 per thousand live births, when recorded as a percentage death rate, gives 0.65 per cent. for live births.

Since not all infants are born alive (and some births are twin births, and so on), a somewhat different rate is to be expected when the maternal death rate is figured in percentage of the total number of women delivered. Also, in hospital practice, at least as commonly conducted at the present time, the disproportionate number of difficult and pathologic cases may be expected to overbalance the advantages of hospital care for the more normal cases.

Hendry[5] reports a maternal mortality of 1.21 per cent. in a series of 6,982 deliveries in a hospital in the course of eight years. Eclampsia and pneumonia each caused (approximately) 20 per cent. of the deaths; septicemia, complications attending cesarean section, and rupture of the uterus, each 10 per cent.; shock, pulmonary embolus and placenta previa, each 5 per cent.; other causes completing the list.

Greenhill,[6] has reviewed the gross mortality among 10,000 parturient women (Chicago Lying-In Hospital), and found a rate of 0.39 per cent.; i. e., thirty-nine cases in all, twenty of them in primiparae and nineteen in multiparae. The causes of death in these thirty-nine cases were: puerperal sepsis (septicemia) and shock, each six cases; pneumonia and embolism, each four cases; toxemia and cardiac decompensation, each three cases; and coronary thrombosis, status lymphaticus, and pulmonary edema, each one case.

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[3] J. A. M. A. **79**:1345 (Oct. 14) 1922.

[4] J. A. M. A. **79**:2172 (Dec. 23) 1922.

[5] Hendry, W. B.: Maternal Mortality, Canadian M. A. J. **13**:252 (April) 1923.

[6] Greenhill, J. P.: Maternal Deaths Among Ten Thousand Parturient Women at Chicago Lying-In Hospital, Surg. Gynec. & Obst. **35**:614 (Nov.) 1922.

One notes in this series the absence of eclampsia, rupture of the uterus, placenta previa and cesarean section as causes of maternal death.

Holland[7] asserts that complications of labor account for 51 per cent. of fetal deaths, the postmortem evidence consisting, as a rule, in cerebral or visceral hemorrhages. In half the cases, he says, the tentorium cerebelli has been torn. Of dead fetuses, after normal breech delivery, this condition has been found in 88 per cent. It has been taught that delivery of the after-coming head should be hurried for fear of pressure on the cord. If, however, death in such presentations is commonly due to a too rapid and forcible molding of the head, better practice, says Holland, would allow the head more time, even as much as ten minutes, if necessary.

The importance of syphilis as a cause of neonatal death has long been known; and its prominence in hospital statistics was emphasized by Williams several years ago.

In a study of the effect of treatment on pregnant syphilitic women and on the life of the child, Williams[8] has recently analyzed the histories of ninety-six treated women (113 pregnancies). Only nine pregnancies ended in abortion and six in premature labor; and, in all these, it seemed permissible to assume that syphilis played no part in the unfruitful outcome. Four infants were born dead or died during the puerperium, and showed signs of congenital syphilis. Of the ninety-eight children remaining, four died from accidents of labor—one premature separation of the placenta, one prolapse of the umbilical cord and two craniotomies—the necropsy in no instance revealing signs of syphilis.

In the 113 pregnancies in syphilitic women, ninety children were discharged from the clinic in apparently good condition. It proved possible to trace eighty of these children: seventy-one were well and gave a negative Wassermann reaction; four could not be tested owing to parental objection, but seemed well; three children had died from pneumonia and one from gastro-enteritis, and one syphilitic child was found.

A review of the maternal data shows that almost ideal results follow anything like efficient treatment of syphilitic women and that surprisingly good results sometimes follow what in men or nonpregnant women would ordinarily be regarded as altogether inefficient treatment. It would seem that there must be something about the pregnant condition which mitigates the virulence of the disease and predisposes to spontaneous cure.

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[7] Holland, E.: Intranatal Deaths, Brit. M. J. **2**:588 (Sept. 30) 1922.

[8] Williams, J. W.: Influence of Treatment of Syphilitic Pregnant Women in Incidence of Congenital Syphilis, Bull. Johns Hopkins Hosp. **33**:383 (Nov.) 1922.

INFANT FEEDING

Figures presented by Vaughan,[9] recently, led the editor of *Hygeia* to proclaim that "during the summer months cholera infantum is the cause of death of more babies than any other disease" and that Dr. Vaughan's data "are undoubted proof that in about six cases of seven the death can be traced to the mother's inability or voluntary failure to nurse her child."

The Children's Bureau of the U. S. Department of Labor insists that, when the importance of the subject is considered, statistical evidence of the relative influence of artificial and breast feeding in infant mortality seems surprisingly meager, most of the data relating to foreign cities or districts.

Data obtained by the Bureau on the mortality of more than 22,000 live-born infants in eight representative cities of the eastern United States, and extending from birth to the first birthday, show that artificial feeding as actually practiced in typical American city populations is associated with an infant mortality between three and four times as high as the mortality among breast-fed infants.[10] The relation appears in all nationalities and in all income groups, though with variations, depending probably on particular conditions prevailing in the groups. If the first nine months was considered, rather than the first year, artificial feeding was accompanied by a five-fold death rate as compared with breast feeding. The ratio was higher (6.3:1) in the group with earnings of $1,250 and over.

An interesting comparison with these figures would be afforded by impartially collected data from the practice of well-trained pediatricians.

Dietrich,[11] of Los Angeles, has analysed 1,000 cases of infant feeding seen almost consecutively in private practice drawn from the American middle class. He found 37 per cent. of infants were nursed three months or less, and 40 per cent., eight months or more. Nine per cent. of the mothers deprived their infants of breast milk within eight days of birth.

In only 8.4 per cent. of the cases in this series were complemental feedings advised and given. Where complemental feedings were given, breast feeding was usually continued another three to five months.

Modified cow's milk (without the addition of a proprietary food) was used as the artificial or substitute feeding in 72 per cent. of the cases. If certain cases in which goat's milk was given are included, 75 per cent. of the infants in the series were started on milk without proprietary foods.

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[9] Vaughan, V. C.: Hygeia **1**:145 (June) 1923.

[10] Woodbury, R. M.: The Relation Between Breast and Artificial Feeding in Infant Mortality, Am. J. Hygiene **2**:668 (Nov.) 1922.

[11] Dietrich, H.: An Analysis of a Series of Case Records Relative to Certain Phases of Breast Feeding, J. A. M. A. **79**:268 (July 22) 1922.

The remaining 270 infants were fed as follows: on condensed milk, 105; milk and Mellin's food, 42; goat's milk, 36; malted milk, 29; milk and Eskay's food, 27; Dryco, 9; other condensed milks 9; Dennos, 8; Nestle's, 6; peptogenic, Allenbury's, and Mammala, 2; Klim, malt soup, Sunbright, each 1.

Rearrangement of these figures shows that 756 infants were started (early or later) on cow's milk or goat's milk, with, no doubt, usually the addition of water and sugar in some form; 114 on condensed milk; 75, or more, on cow's milk with the addition of cereal derivatives (Mellin's, Nestle's, Eskay's, etc.); and approximately 29 on malted milk, and 12 on dried milk (Dryco, Klim, Mammala, etc.).

Years ago Dr. Holt,[12] writing of "infant foods," said: "They add little or nothing to our resources in infant dietetics; in fact, they tend to retard rather than to advance our knowledge of the subject." And recently it has been said: "There is a science of infant nutrition and a few simple foods, such as sweet and sour milk, with curds and sugar, comprise the entire useful armamentarium." Marriott [13] holds that the indications for the use of these are simple and readily understood by any one; and that the apparently brilliant results from various unusual and complicated formulas can always be explained on the basis of the underlying principles and could have been accomplished just as well by simpler means.

The reasons given for weaning, as ascertained in 337 of the 371 cases in which the infants were weaned during the first three months, as tabulated by Dietrich,[14] yield the following figures: insufficient milk, 69; poor milk, blue and watery, 35; insufficient gain, 29; acute illness of mother, 26; green stools and "bad stools," 26; milk dried up, 18; nervousness of mother, 10; abscess of breast, 9; bad milk—poison milk, 7; menstruation, 7; death of mother, tuberculosis of mother, weakness of mother, cracked nipples, and vomiting, each 6; inverted nipples and child's refusal to nurse, each 5; refusal of mother to nurse, not having nursed previous children, toxemia in mother, operation on mother, pregnancy, each 4; prematurity, and inability to nurse, were given as a reason twice, as was cleft palate; and pylorospasm, once. Other infrequently assigned reasons made up a total of fifty reasons advanced for weaning in 1,000 cases seen almost consecutively in private practice.

When rearranged, these data for 337 cases give the following approximate and very suggestive figures: insufficient milk, "poor milk," and insufficient gain, given as reasons for weaning in 132 cases; acute illness in mother, 26; bad stools, 26; abscess of breast and "poor milk," 16; death of mother, tuberculosis, weakness of mother, pregnancy and cleft palate, 23.

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[12] Holt, L. E.: Diseases of Infancy and Childhood, D. Appleton & Co., New York, 1911.

[13] Marriott, W. McK.: Teaching of Infant Feeding, Southern M. J. **15**:530 (July) 1922.

[14] Dietrich, Henry: Footnote 11, p. 269.

In other words, more than one third of the babies were weaned before three months, and about two fifths of these were weaned for reasons having to do essentially with the quantity of the breast milk; one fifth as many more because of supposedly significant, or significant, faults in the appearance of the stools, and one fifth because of acute illness in the mother.

The importance of more general and careful study of complementary feeding is emphasized. Nor should slight apparent abnormalities in the stools of a breast-fed infant be regarded as equal in significance to changes in the stool of the bottle-fed.

Another mortality report, among artificially fed babies, averaging between three and four times that among breast-fed babies, is found in the report of the Children's Bureau on a study (in Baltimore) of the influence of industrial employment of mothers on infant mortality.[15] Previous reports have shown a definite relation between income and infant mortality. This newer study, based on larger numbers, shows that, even in the same income group, the mortality rate is higher for babies when mothers are employed outside the home.

Among the babies included in this study, the mortality rate for the first year of life was one and a half times the rate among babies of mothers not employed. A much larger proportion of the infants were artificially fed when the mothers were employed away from home, and the mortality among these was between three and four times that among breast-fed babies.

A small family income (father earning $450 or less) led to 29.2 per cent. of the mothers in these families being gainfully employed away from home during pregnancy, and 22.1 per cent. during the infant's first year of life. When there was a larger income (father earning $1,200 or more), 1.2 per cent. of the mothers worked out during pregnancy and 0.6 per cent. during the infant's first year.

Employment of the mother during pregnancy was associated with a higher stillbirth rate (more than twice as high), a higher premature rate (6.2 per cent. of the live births, as against 5.7 per cent.), and a higher mortality for the first month of life (77.3 per cent., as against 39.9 per cent.).

Nearly 40 per cent. of the employed mothers worked until within two months of confinement, and 25 per cent. until within two weeks of confinement.

In evaluating the data obtained in studies of this kind, it is obviously difficult to separate the effects of industrial employment, as such, from the results of lower family or group intelligence (measurable in some part by the lower earning power of the father), and squalor and indifference.

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[15] J. A. M. A. **80**:948 (March) 1923.

Rott [16] sees a significant reduction in the percentage of deaths from intestinal diseases in infants, due to the fact that during the war more infants were breast fed.

Bailey [17] writes that in order to prevent premature births the care of the prospective mother must include a reduction of her manual work during the last month of pregnancy, and insistence on a dietary composed largely of carbohydrates.

As a preventive of the high death rate in the neonatal period, he suggests that in maternity hospitals the new-born be turned over to the pediatrician.

Waldstein,[18] in an exhaustive review of the problem of voluntary birth control, considers the number of births and miscarriages reported in the years 1860-1915. In Germany and Vienna, there was a drop in the absolute number born. If miscarriages are considered, it is found that statistics extending over seventy years (commenced by Hegar and Bumm in Germany) show that at least 10 per cent. of all pregnancies terminate in abortion. Study of a series of from 600 to 1,000 or more women indicates that during the twenty-five years of fecund life (from 20 to 45) each woman was pregnant every four years. Waldstein contends that it is natural selection (miscarriage and infant mortality) that tends to keep down the number of individuals.

Hellmuth and Wnorowski [19] show from extensive material that the differences in weight of the new-born at different seasons do not exceed limits covered by statistical work.

Schlossmann,[20] in a study of 13,803 infants in eighteen years, does not find any marked influence of season.

Smith and Merritt,[21] by successive weighings of nursing infants, find that they get the greater part of their feeding of breast milk in the first few minutes, from 40 to 60 per cent. in the first two minutes and from 60 to 80 per cent. in the first four minutes; and that this holds true whether the supply is abundant, moderate or scanty. It is sug-

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16. Rott: Mortality of Infants During the War, Klin. Wchnschr. **1**:381 (Feb. 18) 1922.

17. Bailey, H.: Application of Metabolism Studies of Fetal and Neonatal Periods of Life, Am. J. Obst. & Gynec. **3**:591 (June) 1922.

18. Waldstein, E.: Birth and Miscarriages, Wien. klin. Wchnschr. **36**:131 (Feb. 15) 1923.

19. Hellmuth and Wnorowski: Seasons and Weight of the New-Born, Klin. Wchnschr. **2**:75 (Jan. 8) 1923.

20. Schlossmann: Influence of Vitamin A on Weight of New-Born, Klin. Wchnschr. **2**:304 (Feb.) 1923.

21. Smith and Merritt: Rate of Secretion of Breast Milk, Am. J. Dis. Child. **24**:413 (Nov.) 1922.

gested that there is no good reason why a bottle feeding should not be taken in about the same time.

Bakwin[22] has studied the initial loss of weight in new-born babies, correlating weight changes, skin elasticity and serum protein concentration (plasma water). He finds that usually a marked loss of weight in a new-born baby is accompanied by a loss of skin elasticity and an increase in the serum concentration (indicating a diminution in skin and plasma water), though other babies, despite relatively large weight losses, show no evidence of dehydration of the skin or plasma (presumably owing to a high water reserve in the tissues at birth). Again, impairment of skin elasticity often occurs without increase in plasma concentration, and vice versa. Also, the plasma water percentage may increase even though there is no increase in weight.

Cowie[23] would simplify artificial feeding of infants by allotting an ounce of sugar to each day's feeding and, regarding all sugar as 120 calories per ounce, deducting this from the total calory needs (weight in pounds × 45) and supplying the remaining calories from milk (at twenty-one calories per ounce of 4 per cent. milk). For example, a 10-pound infant would require 450 calories: 120 supplied by the sugar, leaving 330 to be supplied by 15½ ounces of milk. Water is added to give the desired bulk. In actual handling of a case, cereals and vegetables are necessary after the eighth month.

Levy[24] asserts that even in the first three months a more concentrated (two-thirds) milk is better tolerated than milk which has been diluted to one-half. He bases his opinion on a study of 195 cases.

Epstein[25] describes his experiences in giving from one to three teaspoonfuls of porridge daily to infants who required complementary food, or to combat constipation. It proved very satisfactory. The stomach, it is said, contracts around the more solid food, and thus prevents swallowing of air and explosive contractions, which lead to vomiting. The advantage of giving a food less fluid than milk to infants with habitual vomiting seems established.

The use of boiled butter (Lowenbury), butter-soup (Brown and others), butter-flour mixtures (Gismondi) and butter-flour pap (Ernberg) are the subjects of other papers.

Variot[26] declares that infants brought up on sweetened milk evaporated at 50 C. develop normally, other things being equal; and that his experience with 5,000 infants shows that scurvy need not be feared with this form of feeding. Unsweetened condensed milks are heated to too high a point.

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[22] Bakwin, I. H.: Dehydration in Newly-Born, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

[23] Cowie, D. M.: Simple Practical Method for Feeding Infants, Michigan State M. J. **22**:10 (Jan.) 1923.

[24] Levy, J.: Dilution of Milk in Infant Feeding, Deutsch. med. Wchnschr. **48**:1578 (Nov. 24) 1922.

[25] Epstein, B.: Porridge in Infant Feeding, Jahrb. f. Kinderh. **98**:85 (April) 1922.

[26] Variot, G.: Comparative Values of Condensed Milks, Bull. et mém. Soc. méd d. hôp. de Paris **46**:838 (May 26) 1922.

Luttinger[27] urges the use of honey for sugar in infant feeding. It is in largest part fructose (levulose, a levorotatory monosaccharid), rapidly absorbed, and less easily decomposed. It loses its laxative effect on boiling. It has a protein content, from pollen. Luttinger uses it in marasmus, rickets, scurvy and malnutrition; and his experience in more than 400 cases leads him to plead for its more general use.

Clark and Collins,[28] after a study in Boston for the United States Public Health Service, "to determine the safety, usefulness and comparative value of dried milk powder in infant feeding on a practical community-wide basis," say that powdered milk, and especially the whole milk powder, can be safely used for feeding infants when a good grade of fresh cow's milk cannot be obtained. Commercial processes of drying milk are not necessarily destructive of vitamin C, but the use of fruit or vegetable juices is wise.

Poulsson[29] concludes that fat-soluble vitamin A may be administered to breast-fed children through the mother. In a case described, the infant's growth seemed to be arrested at the age of 6 weeks. When the mother began taking a tablespoonful of cod liver oil, three times a day, the infant began to thrive. The mother's milk had always had a normal fat content.

Davison[30] declares that if yeast has any real value in causing an infant to gain in weight, it should be in feeding patients who are convalescent from acute intestinal indigestion or infants suffering from nutritional disturbances such as chronic intestinal indigestion (celiac disease), or physically retarded children. However, feeding yeast (from one-fourth cake to one-half cake a day) to nine infants for from eight to twenty-three days, was without good effect, and in some of the patients abdominal distention occurred, and the stools became frequent.

Rosenstern and Lanter[31] present evidence that the form of solution, the scale of dispersion of the elements of a food rather than its chemical composition, may be of decisive importance in its action on the bowel. In a study of the behavior of crystalloids, colloids, suspensions and

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27. Luttinger, P.: Bee's Honey in Substitute Infant Feeding, New York Med. Rec. **116**:153 (Aug. 2) 1922.

28. Clark, T., and Collins, S. D.: Dried Milk Powder in Infant Feeding Pub. Health Rep. **37**:2415 (Oct. 6) 1922.

29. Poulsson, E.: Fat-Soluble Vitamin A, Norsk Mag. f. Laegevidensk. **84**:35 (Jan.) 1923; abstr., J. A. M. A. **80**:812 (March 17) 1923.

30. Davison, W. C.: Failure of Yeast Therapy in Feeding Infants, Am. J. Dis. Child. **24**:339 (Oct.) 1922.

31. Rosenstern, J., and Lanter: Physical Properties of Food, Ztschr. f. Kinderh. **32**:316 (May 15) 1922.

emulsions, they show that colloids and fine suspensions seem to check diarrhea. Albumin (albumin milk and buttermilk) checks diarrhea, both by its physical and by its chemical properties, while sugar, both physically and chemically, promotes diarrhea.

The length of time which food ordinarily remains in the digestive tract of infants has been studied by Kahn,[32] who concludes that it varies between four and twenty hours, with a usual duration of fifteen hours. The duration is as a rule briefer in breast-fed than in bottle-fed infants. Ordinarily, the figures for the large and small intestines are about the same.

In the prematurely born, the passage averages twelve hours; in dyspeptic babies, from six to ten hours. The difference in passages of shorter duration is chiefly due to more rapid emptying of the small intestine.

BIRTH INJURIES

The various ill-effects to the infant incident to premature and normal birth received considerable attention in the literature of the past year. Hess [33] designates as premature all infants who are born before the end of the normal term of pregnancy (forty weeks), though in common usage the term refers only to those whose gestation period was 260 days or less. He would place in practically the same category congenitally diseased infants, the weaklings, infants born at term, or nearly at term, who have suffered more or less severely during their intra-uterine existence through factors which interfered with their nutrition, and consequently, with their development. He notes the frequent need of orthopedic treatment in these cases.

The low coagulation point and prolonged bleeding time observed in the blood of premature and other new-born infants is emphasized in recent writings.

Munro and Eustis [34] propose the following etiologic classification of cases of intracranial hemorrhage in the new-born: (*a*) traumatic group; (*b*) "asphyxia" group; (*c*) fetal disease group. They would base the diagnosis of intracranial hemorrhage in the new-born on the result of the following determinations: (*a*) history and physical examinations; (*b*) measurement of intracranial pressure by spinal manometer; (*c*) determination of the coagulation and bleeding times.

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[32] 32. Kahn, W.: Ueber die Dauer der Dormpassage im Sauglingsälter, Ztschr. f. Kinderh. **29**:321 (July) 1921; Weitere Mitteilungen über der Dauer der Dormpassage im Sauglingsälter, Ztschr. f. Kinderh. **33**:48 (July) 1922.

[33] 33. Hess, J. H: Premature Infants, J. A. M. A. **79**:552 (Aug. 12) 1922.

[34] 34. Munro, D., and Eustis, R. S.: Diagnosis and Treatment of Intracranial Hemorrhage in New-Born; Report of Fourteen Treated Cases, Am. J. Dis. Child. **24**:273 (Oct.) 1922.

Rosamond[35] thinks a universal routine determination of the blood coagulability would reduce the mortality of the new-born practically 50 per cent., and would probably prevent a large number of cases of birth palsy. Of seventeen cases of convulsions in the new-born seen by him in twelve months, fourteen manifested delayed bleeding-clotting time and were in all probability due to cerebral hemorrhage. One case, in a baby delivered by cesarean section, was marked by absence of all external bleeding; severity of the convulsions, with a duration of thirty-six hours before efforts to stop the hemorrhage were made, and their prompt cessation when bleeding was stopped. The thirteen other cases all responded promptly to blood therapy.

Munro and Eustis would have the treatment of intracranial hemorrhage due to hemorrhagic disease depend on (*a*) the successful etiologic classification of the case and (*b*) the recognition and measurement of the intracranial pressure; and the treatment consists in the administration of normal whole blood subcutaneously until bleeding and coagulation time have returned to normal, and then appropriate relief of the intracranial hypertension.

It will be recalled that Rhodda's method of testing the coagulation time in the new-born consisted in part in placing a drop of blood between two watch crystals and rolling a lead shot through the drop till the shot was caught by the coagulum. He found that the average coagulation time in new-born infants was seven minutes, and ranged from five to nine minutes. He noted that the coagulation time was progressively prolonged till the fifth day, and then returned to normal by the tenth day. Clinically, most spontaneous hemorrhages of the new-born occur in this interval, from the second to the eighth day.

Falls,[36] using essentially the technic of Howell, that his results might be better compared with the figures obtained by others, found that fetal blood at birth clots with normal firmness and rapidity, so that subsequent hemorrhagic tendencies cannot be detected from coagulation tests at this time. At the time of birth, maternal and fetal blood have practically the same coagulation time; and in general the coagulability of the blood of women before, during and after labor, as measured by the estimation of the coagulation time, calcium, and prothrombin content is well within the limits of normal blood coagulability. Use of anesthesia was without effect on coagulation time.

Schwartz,[37] in examining cadavers of infants, found typical focal processes in the brain in 130 infants less than 5 months old, and diffuse pathologic changes in 100 others. In 65 per cent. of all new-born dying within five months, he found effects of birth trauma: hemorrhage and softening that could be discerned with the naked eye. His observations led him to believe that the pathology and pathologic anatomy of earlier infancy are determined mainly by injuries to the central nervous system.

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[35] Rosamond, E.: Intracranial Hemorrhage in New-Born; Case Report, Southern M. J. **15**:618 (Aug.) 1922.

[36] Falls, F. H.: Coagulability of the Blood During Pregnancy and in the New-Born, J. A. M. A. **79**:1816, 1922.

[37] Schwartz, P.: Birth Traumatism of Brain, München. med. Wchnschr. **69**:1110 (July 28) 1922.

Siegmund[38] emphasizes the injury to the vascular system in birth trauma. Mechanical injuries to small vessels, in his view, cause disturbance in the circulation, stasis, and diapedesis of erythrocytes, with impairment of nutrition in adjacent tissue, and resulting degeneration that may lead to necrosis. He states that small foci of softening are found in infants, especially in the premature, within the first six months, and that the fatty degenerative process of neuroglia, known as encephalodystrophia of the new-born, is in the majority of cases due to birth trauma.

Cruickshank[39] reports on a series of 200 mature infants. Hemorrhage was found in about 80 per cent., and gross hemorrhages in 50 per cent., two thirds of which were gross meningeal hemorrhages—and in two thirds of these again, the meningeal hemorrhage was the only gross hemorrhage present, while in the remaining third there were gross visceral hemorrhages also. In approximately one infant out of eight in this series, there was gross visceral hemorrhage without meningeal hemorrhage.

In 200 premature infants (born during the eighth or ninth lunar month of pregnancy), the incidence of hemorrhage was 66 per cent., and of gross hemorrhage, 40 per cent. Gross meningeal hemorrhage alone was less common, being more often associated with gross visceral hemorrhage; and gross visceral hemorrhage alone occurred more than twice as often in mature infants.

A much smaller series of neonatal deaths is reviewed by Capen.[40]

Cameron and Osman[41] state that, among cases of infantile diplegia or paraplegia, it is possible to recognize a group in which the defect is confined to the sensorimotor cortical areas; that since education at first proceeds almost entirely by sensorimotor paths, there is, in early childhood, a deceptive appearance of gross mental defect; later, progress may be rapid and recovery almost complete. Incoordination may remain, and voluntary movements may be stiff and awkward, though character and intelligence may be on a high plane.

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[38] Siegmund, H.: Birth Injuries and Their Consequences, München. med. Wchnschr. **70**:137 (Feb. 2) 1923.

[39] Cruickshank, J. N.: Hemorrhages of New-Born, Lancet **1**:836 (April 28) 1923.

[40] Capen, N. B.: Intracranial Trauma in the New-Born, J. Obst. & Gynec. **29**:572, 1922.

[41] Cameron, H. C., and Osman, A. A.: Late Results of Meningeal Hemorrhage of the Newly-Born, Brit. Med. J. **1**:363 (March 3) 1923.

Shoemaker [42] reports an instance of hemorrhagic disease of the new-born, with notes on successful treatment. Bleeding began on the third day, with vomiting of much bright red blood, followed by passage of dark blood and clots by bowel. Loss of blood recurred at intervals through three days, causing the infant to become cyanotic and cold, and the respirations shallow to imperceptibility. As a result of his experience, Shoemaker concludes that calcium lactate is of practically no value in this emergency; that thromboplastic serum, in any of the commercial forms accepted by the Council on Pharmacy and Chemistry, acts promptly as a hemostatic agent if used in sufficiently large doses (in this instance, 10 c.c. was used); that it should be followed, whenever possible, by whole blood transfusion, without loss of time. In his case, whole blood from the father was given by direct transfusion, from the median basilic vein into the longitudinal veins of the infant through the anterior fontanel.

Losee [43] thinks the clinical picture of cerebral hemorrhage in the new-born is usually sufficient to establish a definite diagnosis, and that lumbar puncture will determine the diagnosis sometimes in doubtful cases. The value of lumbar puncture in draining blood from the subarachnoid space depends on conditions; the success of the operation for decompression depends on the location and extent of the lesion. He reports sixteen cases of hemorrhage of the new-born treated by blood transfusion. Eight had been earlier treated with normal human serum without any result, and in one, the hemorrhage occurred after blood transfusion. There were seven cases of subcutaneous hemorrhage; three of cerebral hemorrhage following operative delivery; three of hemorrhage from the umbilicus; two with gastro-intestinal hemorrhage, and one from the wound following circumcision.

Ballance [44] reports a case of difficult forceps delivery with frontal bone fracture and intracranial hemorrhage. An operation was performed on the fourteenth day. A broken fragment had allowed blood to escape from within the cranial cavity to beneath the scalp. The depressed fragment was removed, and the child made good recovery. Six weeks later, no opening in the skull could be detected.

In a consideration of spina bifida and encephalocele, Hess,[45] in saying that the condition is essentially surgical, states that operation may frequently be delayed through frequent paracentesis, with intermittent indications for operation. Hydrocephalus frequently accompanies spina bifida or follows operation.

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[42] Shoemaker, J. A.: Hemorrhagic Disease of the New-Born with Direct Transfusion into the Longitudinal Sinus Through Anterior Fontanelle, J. A. M. A. **79**:1608 (Nov. 4) 1922.

[43] Losee, J. R.: Hemorrhage in the New-Born, Bull. Lying-In Hosp. New York **12**:100 (July) 1922.

[44] Ballance, A. C., and C. A.: Intracranial Hemorrhage in the New-Born; Fracture of Skull of Infant, Lancet **2**:1109 (Nov. 25) 1922.

[45] Hess, J. H.: Footnote 33, p. 553.

For the relief of this in cases that have come under his observation, drainage into the subdural space, under the scalp, into the jugular veins, and puncture of the corpus callosum, have given little more than temporary relief. In a series of six cases observed recently, a cylinder of cortex, about three eighths of an inch (0.9 cm.) in diameter, was removed from the frontotemporal region. The plug of cortex extending into the lateral ventricles was removed with a piece of glass tubing having a sharpened edge, after the skull was opened at a lateral angle of the large fontanel and the dura incised and sutured to the arachnoid. The six infants are all living, with no visible evidence of disturbance of sensation or of muscular power. In experimental animals, the defect in the cerebral cortex remained permanent in five out of seven cases, and, in some of them, the lumen was found at necropsy to be lined with epithelium, probably from the lateral ventricles.

It is also stated that paraplegias or diplegias have been reported in more than 3 per cent. of all surviving premature infants; that mental defects in premature infants are, in at least 75 per cent. of all cases, accompanied by spastic monoplegias, paraplegias, or diplegias, and that these figures would be much higher were it not that most of the premature infants suffering from injuries to the brain die very early. Traumatic injuries from labor are seen in a greater percentage of premature infants than of full-term infants. The symptoms are less evident, and roentgenograms should be made in very doubtful cases.

METABOLISM

The metabolism of the new-born has been studied by a number of workers. The problem is a difficult one and seemingly contradictory views are expressed. Where adults have a basal metabolism of approximately 1 calory per kilogram of body weight for each hour, or 24 calories a day, children less than 1 year old may show 50 or 60 calories. In normal recently fed infants, the heat production may reach 60 calories per kilogram a day. New-born infants have been found to have a lower metabolism, perhaps not exceeding 48 calories per kilogram. Difficult questions as to whether the comparisons shall be made on the basis of body weight or body surface enter in. Figures recently obtained by Talbot and his co-workers[46] indicate that the basal metabolism of premature but organically sound babies is startlingly low from any point of view.

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46. Talbot, F. B.; Sisson, W. R.; Moriarty, M. E., and Dalrymple, A. J.: Basal Metabolism of Prematurity. II. Relation of Basal Metabolism to Calorie Intake and Weight Curve, Am. J. Dis. Child. **24**:95 (Aug.) 1922.

This was true in seven of twenty-two premature infants studied by them, who did not gain in weight until they were able to digest approximately 200 calories in the day. A relatively large proportion of the food went to form new body tissue, and less was available for heat production. In the view of these authors, the large excess of the caloric intake over the basal metabolism was necessary because of the relatively great amount of growth essential for the normal development of these babies. Rubner and Langstein (1915) found more than 40 per cent. of the calories ingested as food was retained in prematurely born infants. Talbot and Sisson believe that the amount of heat formed depends on the amount and tone of the active "protoplasmic" tissue, and not primarily on the size of the surface of the body in these infants, and that the active, heat forming, protoplasmic tissues are unable to respond to the excessive heat loss; hence, the subnormal temperature. Talbot's patients did not gain until they were able to digest approximately 200 calories daily, and the only food completely assimilated was human milk.

Hoffa[47] reports other findings. She compared results in normal premature infants given a minimal amount of food with results in others fed abundantly. All were healthy infants of healthy parents. They were fed with pumped breast milk, gradually supplemented with buttermilk. No incubators were used. Many infants were studied, but data are given from eleven cases in the first group and two in the second.

The charts are held to show that, at least in many cases, the actual requirement is less than 100 calories per kilogram. These infants sleep, and scarcely move, and use up very little energy. This physiologic need of rest Hoffa respected by feeding through a stomach tube left in place continuously in the nose, being fastened with adhesive plaster. The milk was slowly increased up to 100 calories per kilogram, and this figure was not overstepped till ten or fourteen days had elapsed without further increase in weight. The growth in weight and length was satisfactory in all. One infant had doubled its birth weight by the twelfth week. All these infants fed on minimal amounts improved with a regularity that was attributed to lack of digestive strain on account of their getting only the nourishment needed, without any excess. Contradictory statements in the literature are explained by the fact that previously congenitally feeble and normal premature infants have been grouped together.

CHILD WELFARE

In a consideration of the basic aims of the child hygiene movement, Veeder[48] groups the methods so far employed under three headings:

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[47] Hoffa, L.: Requirements in Calories of the Prematurely Born,' Arch. f. Kinderh. **72**:6 (Sept.) 1922.

[48] Veeder, B. S.: Child Hygiene and the Private Physician, J. A. M. A. **79**:2228 (Dec. 31) 1922.

(1) the use of specific means, as, for example, the crusade for pure milk, or the use of toxin-antitoxin in diphtheria; (2) educational methods, including such diverse items as propaganda through the press, the holding of health exhibits, the teaching of health habits to groups of children in the schools and the visitation of the home by health workers, and (3) the direct supervision of the infant and child by the physician through clinics, or—a better term—welfare conferences.

Veeder finds certain inherent basic defects in the welfare conference. First, experience having shown that the welfare conference must confine itself to the well child, since sick and well children should not mingle and the presence of a sick child attracts a disproportionate share of the attention of the conference, the conference physician is deprived of that observation of the child when sick, which in many instances is the most important factor in determining what to do when the child or infant is well.

Second, the conference physician fails to see the child in its normal, every-day surroundings, and there is a close and intimate relationship between the physical condition of a child and its environment. Attempts to see this environment through an intermediary, a nurse or a social worker, are at best unsatisfactory and incomplete substitutes for personal observation.

Again, there is an element of weakness in the changing personnel of the conference, and in the child's passage from one conference to another as he advances in age.

Finally, welfare clinics are classed as "charities," and limited in their work to the poor; whereas, there is just as much need of health work among the children of the middle and well-to-do classes of society.

In Veeder's opinion, the best results can be obtained only if there is direct and constant supervision of the child through infancy and childhood by one physician, who sees the child in sickness as well as in health, and who has an intimate and personal knowledge of its parents, its home life and daily environment, its play and companions.

Such a man should be the physician in general practice. That he is lacking in knowledge concerning the hygiene and development of normal infants and children is the fault of the physician's training, not of the physician.

However, if the principles and practice of child hygiene are as important as they are believed to be, the situation, in Veeder's opinion, will automatically correct itself in time.

Emerson[49] holds that the forces affecting the child's health which must be coordinated to insure success are: the home, the school and other agencies; medical care, and the child's own interest. Summarized, his program consists of (1) weighing and measuring as a means of identification; (2) diagnosis based on complete physical, mental and social examination; (3) removal of physical defects as a prerequisite for successful treatment; (4) measured feeding (forty-eight hour diet record); (5) midmorning and midafternoon lunches; (6) midmorning and midafternoon rest periods; (7) regulation of physical, mental and social activities to prevent overfatigue (forty-eight hour list of activities); (8) nutrition classes for the treatment of malnutrition; (9) nutrition or diagnostic clinics for problem cases (average weight for height to be used as a minimum standard of nutrition and growth).

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[49] Emerson, W. R. P.: Nutrition and Growth in Children, Boston M. & S. J. **188**:8 (Jan. 4) 1923.

In a study of the effect of living conditions on schoolchildren of large cities, Kurcharski (Berlin Letter, J.A.M.A. **79:** 2178 [Dec. 25] 1922.) had a comprehensive questionnaire filled out by more than 1,300 children, belonging mainly to the poorer classes of an outlying section of Berlin. Only 8 per cent. of the children were in a good state of nutrition, 21 per cent. were much undernourished and 16 per cent. were mentally backward, judging from their achievements in school. While it was shown that unfavorable social conditions, such as overcrowded apartments, lack of employment of the father and inadequate care on the part of a working mother, exerted a harmful effect on the mental development of the schoolchildren, it could not be shown that any damage to physical development had occurred as a result of these conditions.

A report of the United States Department of Labor [50] on the children of wage earning mothers (Chicago) covers 2,066 children in 843 families, one fourth of them colored. Overfatigue and illhealth were found in the mothers. In the children, retardation of school progress—more of the children were below the standard grade for their age—was found, and, in some instances, overwork by children who had responsibility for household tasks beyond their strength. Remedial measures are those looking toward reducing the necessity for wage earning by mothers of young childen; i. e., improvement in economic conditions that will make the fathers' earnings more nearly adequate; training of the mothers in household management and the care of children, and preserving the family group through social measures (prevention of accidents, promotion of health, mother's pensions, etc.).

Pearson,[51] as the result of a statistical study, holds that, on broad lines, health and intelligence are innate and are chiefly controlled by inheritance; that health and intelligence are correlated though not markedly; that general health changes very little during the whole school period; that it does not seem feasible in the present state of medical knowledge to improve intelligence by modifying health; that it is the intelligent rather than the slow or dull children who exhibit athletic power; that general intelligence and a variety of psychic characters remain unchanged throughout the whole range of school life, and that health is associated only in a minor degree with certain psychic characters.

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[50] Children of Wage Earning Mothers: A Study of a Selected Group in Chicago, Rep. U. S. Dept. of Labor.

[51] Pearson, Karl: Draper's Company Research Memoirs, London Letter, J. A. M. A. **80:** 1861 (June 25) 1923.

In a study of elementary grade schoolchildren in a typical American community, Sterling[52] found that the school work had little if any adverse effect on the pupils' weight, and that the under-age child (school entrance here, 6 years) made as good a showing in this respect as the normal age or average child. It is apparent that school life, apart from detrimental influences which may exist in the home environment, is not ordinarily harmful to the child's state of nutrition.

In England, a consultation committee[53] that included Dr. J. S. Adami notes that, up to 1850 or later, it was assumed that the education of girls must be different from that of boys because they belonged to a "weaker sex." Then it came to be held that it should be based on their equality. Now it is coming to be recognized that equality does not demand identity but is compatible with and even depends on a system of differentiation.

The committee recognizes that most boys, especially at adolescence, have a habit of "healthy idleness," and thus can protect themselves against overpressure; whereas girls, being more amenable to authority and more industrious, are more liable to overfatigue, in studies and in sports. It is recommended that the first school examination for girls should be about a year later than for boys; that school physicians and others give more attention to protecting girls against physical fatigue and nervous overstrain, and that, in girls' day schools, in some instances, the amount of home preparation should be reduced, in view of domestic duties.

In a lengthy paper on the mental and physical health of school children, Sanger Brown, 2d.[54] doubts that Goddard's contention (in "Human Efficiency and Levels of Intelligence") that efficiency and success in life are largely dependent on intelligence and that failure is due to a lack of it is exactly the case. Many people with high intelligence do not succeed; while others with inferior intelligence, through their pleasing personality and adaptability in getting along with people, do relatively well.

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[52] Sterling, E. B.: Nutrition and Education, Pub. Health Rep. **37**:2798 (Nov. 10) 1922.

[53] London Letter, J. A. M. A. **86**:414 (Feb. 10) 1923.

[54] Brown, Sanger: Mental and Physical Health of School Children, J. A. M. A. **80**:1351 (May 12) 1923.

He pictures at some length the complex character of the child's education in the preschool years, his acquirement of control of his body, of patience and selfcontrol and of social adaptability. The success with which this early development in physical, mental and social spheres is accomplished is tested, in most cases, when the child enters school.

The great majority of children do reasonably well, he thinks, in the schools of today, but the fact remains that a certain percentage get along indifferently, or not at all. Of this small group, some are physically below par, some acquire slowly, some are remarkably brilliant and some have the makings of genius in them. His observations are based on a survey of 150 of these cases. Such children are usually spoken of as difficult or unusual. At one time, it was thought that mental defect was the basis of most of the difficulty, and reports were made which showed that from 60 to 80 per cent. of the conduct disorders of children were attributable to mental defect. Now, some difficult children are found to be defective; but by no means the majority. Some suffer from malnutrition, but some are perfect physical specimens.

In this survey, nervous symptoms were found in 20 per cent. of the group; epilepsy in four instances, and various nervous symptoms in the others. States of anxiety and fear, night terrors, stammering in several cases, and overactivity were found; also instances of undue sex stimulation before puberty, and nervous instability from undue fear of competition in school.

One third of the group had some type of visual defect, some requiring glasses. A few cases of defective hearing were found, the result of former otitis media. Nearly half had enlarged tonsils, in many cases only slightly enlarged and apparently causing no symptoms; but in a number there was associated difficulty in nasal breathing, with restlessness at night and night terrors, attributable to the interference with free passage of air. In nineteen cases, there was defective nasal breathing; in some, a mild defect caused by a deviated septum.

Poorly nourished children seemed to suffer in a particular way mentally, being emotionally unstable and having nervous symptoms.

For the relief of these children, appropriate medical and social measures are suggested, and particular forms of education. For the nervous ones, class progress is the less important thing until mental stability is gained. In time, the nervous tension subsides, the worried look disappears, sound sleep returns and the ability to concentrate and learn easily. For the children who are slow, yet have no nervous handicaps, but make a low record by psychologic tests, manual education should be introduced at the age of 11 or 12 years, or earlier, and time not squandered on academic studies.

Heller[55] draws attention to children who are intellectually normal or above normal, but who fail in the motor sphere. They are clumsy in dressing, and do not learn to run, jump or dance gracefully. He advocates individual training, devoted toward bringing the child to understand the mechanical details of such movements, training both mind and muscles.

In a study of defects in 15,605 schoolchildren, Bruce[56] found that at 5 years of age, 58 per cent. of the "crippling" was due to rickets of the most pronounced type; 9 per cent., to tuberculosis (pulmonary tuberculosis being conspicuous by its absence); 7.4 per cent., to nervous diseases; 6.3 per cent., to mental deficiency (retardation?); 6 per cent., to chronic bronchitis, and 3.9 per cent., to anemia and malnutrition without symptoms of other disease. The remaining 9 per cent. of crippling was due to eye conditions (mainly strumous ophthalmia), a few cases of heart disease (the acquired ones due to scarlet fever and rheumatism) and miscellaneous conditions such as congenital and acquired deformities. One notes the high percentage of handicapping due to rickets, tuberculosis (other than pulmonary) and chronic bronchitis, in these British schoolchildren of tender age.

In London, Sir George Newman's report (1921)[57] shows that there are 164,000 "exceptional" children. Of these, the blind number 58,000; the feeble minded, 31,000; the cripples (other than the tuberculous), 23,000; tuberculous cripples, 13,000; those having pulmonary tuberculosis, 2,000, and so on.

In contrast with these figures for children, the conditions found in adult life are of interest. General Ireland[58] states that of all Class I men, more than one young man in five was physically unfit to perform any type of military service either at home or abroad.

The more important causes of rejection were: organic diseases of the heart, 11.5 per cent. of the total causes of rejection; tuberculosis, 9.3 per cent.; errors of refraction, 8.4 per cent.; underweight, 7.6 per cent.; mental deficiency, 4.5 per cent.; hernia, 4.3 per cent.; flatfoot, 3.6 per cent.; defective and deficient teeth, 3.2 per cent., and defective speech and hearing, 2.6 per cent. Many of these conditions obviously reach back into childhood. Many must seem relatively unimportant to nonmilitary men.

Of the large classes of diseases, the defects of the bones and organs of locomotion ranked first, with 17.2 per cent. of the total causes of rejection. Diseases of the heart and blood vessels second, 15 per cent.; diseases of the eye third, 12.6 per cent.; and tuberculosis fourth, 9.3 per cent.

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[55] Heller, T.: Motor Underdevelopment of Children, Ztschr. f. Kinderh. **34**:287 (Jan. 10) 1923.

[56] Bruce, R.: Defects in School Children, Brit. M. J. **2**:346 (Aug. 26) 1923.

[57] London Letter, J. A. M. A. **79**:1700 (Nov. 11) 1922.

[58] Ireland, M. W.: Physical Defects Discovered in Selective Draft Men During the World War, J. A. M. A. **79**:1579 (Nov. 4) 1922.

Nine men out of each hundred had two defects which were of sufficient military importance to note.

Of these same Class I men, more than two out of every five (i. e. 47 per cent.) had a physical defect of sufficient importance to be noted in the reports of the examinations of the local and camp examining boards. Practically all of these defects were of some importance even to those who did not expect to engage in arduous physical exercise or labor. Of the individual defects which were recorded most frequently in the men examined, the principal ones occurred in the following order: flatfoot, 11.7 per cent.; venereal disease, 5.7 per cent.; hernia, 4 per cent.; refractive errors of the eye, 3.3 per cent.; organic disease of the heart, 3.1 per cent.; underweight, 3.1 per cent.; tuberculosis, 2.5 per cent.; hypertrophied tonsils, 2.3 per cent.; defective teeth, 1.4 per cent., and mental deficiencies, 1.2 per cent.

Vercoe [59] has studied the effect of the child's position in the family on his health, relative intelligence, physique and resistance. In comparison with the first, the second, the third child, etc., in the family, there is no appreciable difference between any of the children investigated. In incidence of disease, the eldest child fares definitely the worst, the eighth and upward the best. As far as his series goes, he concludes that the quality of the average child does not deteriorate in any way with successive pregnancies; and the quality of the family does not deteriorate in any way with increase in quantity, in the environment and class under consideration.

On the other hand, Reiter and Ihlefeldt [60] conclude, from a study of 634 legitimate children, that repeated pregnancies and the higher age of the mother influence the somatic and psychic qualities of the child unfavorably.

Edberg [61] estimates that about 130 cases of harelip or cleft palate appear yearly in the 125,000 children born in Sweden. The condition seems to occur in boys 14 per cent. oftener than in girls. Direct heredity of the deformity seems evident in 2.3 per cent. of cases; coincidence in brothers and sisters in 3.7 per cent., and a combination of deformities in 5.1 per cent.

Some evidence of inheritance is also noted in congenital luxation of the hip joint (more common in girls) and in talipes (more frequent in boys).

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59. Vercoe, R. H.: Effect of Position in Family on Health of Child, Lancet **2**:758 (Oct. 7) 1922.

60. Reiter and Ihlefeldt: Influence of Mother's Age on Development of Child, Klin. Wchnschr. **1**:2524 (Dec. 16) 1922.

61. Edberg, E.: Hare-Lip and Cleft Palate, Acta Chir. Scandinav. **55**:1 (July 15) 1922; abstr. J. A. M. A. **79**:1562 (Oct. 28) 1922.

Rosenstern[62] publishes five cases of children who were much smaller than other children of their age, the lack of height being due chiefly to shortness of the lower extremities, and the mutual proportions of the body corresponding to a younger stage. He speaks of such children as exhibiting temporary dwarf growth. Some of the children change later to normal proportions.

Seham[63] finds that the responses to exercise that are encountered in normal children of school age are those that are encountered in adults. The physical capacity of children, as judged by the maximum physical output, is in direct relationship to age, circumference of chest, circumference of thigh and vital capacity. Height and weight do not alter it so constantly.

Emerson[64] believes that there has been a tendency to overrate the importance of corrective exercises; that most cases of bad posture are due to general weakness of a body with too little weight to support its height, and that the first need is a program that will bring the child up to his normal weight.

NUTRITION

In the absence of satisfactory data from other sources, Holt and Fales[65] have employed the statistical method to ascertain the amount of fat that healthy children are accustomed to consume. While many factors, social, economic and otherwise, may tend in civilized life to modify instinctive cravings, data obtained by this method should at least offer a starting point for further studies.

As a result of their investigation, Holt and Fales conclude that, in general, it seems rational to supply in the diet of the child as much as 4 gm. of fat per kilogram daily at 1 year, decreasing the amount to about 3 gm. per kilogram at 6 years, and maintaining this value throughout the growth period. They feel that there is little evidence that a liberal amount of fat in the diet is harmful to children with normal digestion, and much evidence that fat is an important and necessary component of the diet during the entire growth period. Fat is said to exert a protective action against the irritating effects of the products of carbohydrate fermentation. The authors urge that the grounds for the current impression regarding the harmful effects of fat in children be carefully investigated.

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62. Rosenstern, J.: Temporary Dwarf Growth, Ztschr. f. Kinderh. **34**:310 (Jan. 18) 1922.

63. Seham, M., and Egerer-Seham, G.: Physiology of Exercise in Childhood. I. A Study of Normal Children of School Age, Am. J. Dis. Child. **25**:1 (Jan. 1) 1923.

64. Emerson, W. R. P.: Nutrition and Growth in Children, New York, D. Appleton & Co., 1922.

65. Holt, L. E., and Fales, H. L.: Food Requirements of Children. III. Fat Requirement, Am. J. Dis. Child. **23**:471 (June) 1922.

They assert [66] that a diet in which the percentage distribution of the total calories is fat, 35 per cent.; protein, 15 per cent., and carbohydrates, 50 per cent. is one which meets the nutritive needs of the child after infancy, and is well borne by the digestive system, and hence may be considered as well balanced with respect to these elements.

In studying the carbohydrate intake of 100 healthy children from 1 year to 18 years of age, Holt and Fales [67] found an average figure of 10 gm. per kilogram. It is held that a diet that is excessive in carbohydrates leads to an abnormal deposition of fat without corresponding increase in muscle development; that children taking such a diet have feeble resistance to infection; that a relationship exists between the high proportion of carbohydrate in the modern diet and the prevalence of dental caries, and that definite digestive disturbances, chiefly intestinal, may be produced when the carbohydrate in the diet is excessive—there may result increased fermentation with acid, loose stools or constipation with flatulence and abdominal distention, and when long continued these disturbances are very difficult to control.

In an article of popular character on the accessory food factors, vitamins, Dr. Holt [68] notes how greatly the variety and palatability of our food have been increased by the use of such processes as milling, drying, canning, condensing and sterilizing; also the widened distribution of foodstuffs that is made possible, and the protection against local famine. These preserved foods are of great help in the nutrition of both children and adults, and one would not stop the use of them if it were possible. But the increasing knowledge of vitamins has shown that the procedures involved in their preparation have their disadvantages, and even dangers.

When the nature of these disadvantages and dangers is thoroughly understood and their importance appreciated, the remedy will come also. In the food of infants, it is only vitamin C that is likely to be injured. The amount of this vitamin in milk is very small, at best, and the body evidently has a store sufficient to meet its needs for a considerable time, scurvy appearing usually only after an interval of between five and seven months.

Vitamins C and A are abundantly supplied by milk, eggs, green vegetables and fruits, all of which are expensive foods for the poor, but should be included in a nursing mother's diet; and by yolk of egg, the juice of steamed green vegetables and, best of all, by cod liver oil, for the infant. To infants whose principal or sole food is any one of the forms of heated, dried or condensed milk, it would appear quite sufficient if an antiscorbutic were begun at the age of 5 months. In winter time, it would seem a wise precaution to supplement cow's milk, which at that season may be poor in vitamins, with a vitamin-rich food.

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[66] Holt, L. E., and Fales, H. L.: Food Requirements of Children. V. Percentage Distribution of Calories, Am. J. Dis. Child. **24**:311 (Oct.) 1922.

[67] Holt, L. E., and Fales, H. L.: Food Requirements of Children. IV. Carbohydrate Requirement, Am. J. Dis. Child. **24**:44 (July) 1922.

[68] Holt, L. E.: Practical Application of the Results of Vitamin Studies, J. A. M. A. **79**:129 (July 8) 1922.

Holt has never seen or known of a case of scurvy in a child over 2 years of age under normal peace conditions. As to vitamin A, so indispensable for the growth of children, it is necessary only that care be taken that the diet include an ample supply, since it is not likely to be injured in the preparation or preservation of food.

Children should eat a variety of food. Special dangers may follow the habitual use of a very restricted diet. During the entire period of growth, the diet should include, if possible, whole milk, or if skim milk is used, it should be supplemented by butter. Of the butter substitutes, those which contain beef fat, mutton fat and peanut oil are better than those in which vegetable oils or lard are important constituents.

A diet which contains no milk whatever should contain ample amounts of the leafy or green vegetables. The chief objection to cabbage, a rich source of all the vitamins, and cheap, and lettuce and celery, when used in the raw state, is the difficulty of making children masticate them properly.

Cereals, particularly those from whole grains, and potatoes are important and adequate sources of vitamin B.

Fruits have other uses than as laxatives and as sources of mineral salts, and should form a regular part of the diet. When fresh fruits are not available, dried fruits may be given, but they are distinctly inferior to canned tomatoes as sources of the antiscorbutic vitamins.

If the daily diet contains a reasonable amount of unskimmed milk, cereals, potato, green vegetables and fruit, one need not fear a vitamin deficiency.

The place of purin in the diet of children is discussed by Czerny[69] in a paper on natural immunity in children. An infant gets along very well on a food poor in purin. At what age a diet rich in purin must be introduced is a matter of controversy. There are, he says, no doubt, children who will thrive for years on a diet poor in purin, and there are a good many children who need food rich in purin from the time they are 2 years old. The highest susceptibility to disease, combined with a marked tendency to hyperplasia of the lymphatic tissue, is seen in children who subsist for long periods on food poor in purin. As research in metabolism has shown that not every child is able to extract from primitive forms of food all that his organism needs, it is necessary to prescribe food elements in definite known forms, or harm may arise.

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69. Czerny, A.: Natural Immunity in Children, Klin. Wchnschr. **1**:561 (March 18) 1922.

Blatherwick and Long,[70] in studies on urinary acidity, find that the drinking of large amounts of orange juice results, in young women, in the production of alkaline urines, an increased organic acid excretion and a decreased ammonia content of the urines. It was not possible to overreach the organism's ability to oxidize citric acid even though the amounts drunk in one day were the equivalent of about 48 gm. of acid.

The drinking of large amounts of lactic acid milk caused the formation of strongly acid urine, the increased acidity being due to the excretion of increased amounts of acid phosphate, as indicated by simultaneous increase in the titratable acidity and phosphorus. The lactic acid appeared to have been completely oxidized or retained, as there was no change in the organic acid excretion.

In a study of the effect of proteins on bacterial fermentation, Rühle[71] confirms Kayser's and Bluhdorn's observation of increased formation of acid in the presence of proteins. He finds that the figures are still higher if products of peptic-tryptic digestion are used, the stronger fermentation being simply due to a physicochemical binding of acid with the proteins, which enables the micro-organisms to continue the fermentation and produce more titrable acid; but for the same reason this acid does not hurt the mucosa of the intestine, and thus, proteins have no harmful effects in intestinal fermentation.

Buckheim[72] reports findings in roentgen-ray examination of the gastro-intestinal tract in children over 1 year of age, twenty-three cases, and quotes from the literature. On the average, the stomach empties in two hours, and the small intestine in from two to four hours.

Sauer, Minik, and Alexander[73] have studied further the gastric findings in children with anorexia. Some years ago, it was pointed out that one of the pronounced effects of delayed emptying time of the stomach in children is loss of appetite, and that a child will not be hungry with a portion of a previous meal in the stomach.[74] (One must except here certain healthy growing children who seem always to be hungry.)

In this work with underweight children, the authors occasionally encountered children who were free from tuberculosis, anemia, physical defects, diseased tonsils, adenoids and other known causes of anorexia, yet who when given three meals a day, avoiding excess of fats, ate less than the required number of calories, and were underweight because they ate insufficiently. A study was made of the gastric motor and secretory functions in twenty-one such children and twelve normal children. A meal recommended by the Royal Society of Medicine for roentgenographic examination of the alimentary canal was employed. It was given within fifteen minutes, and serial films were made four hours later, and each succeeding hour until the stomach was emptied. Other details as to ingestion, posture and occupation were supervised. Observations were repeated after a few days in a number of subjects in both groups, and in most subjects after a lapse of several months.

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[70] Blatherwick, N. R., and Long, M. L.: Studies in Urinary Acidity. I. Some Effects of Drinking Large Amounts of Orange Juice and Sour Milk, J. Biol. Chem. **53**:103 (July) 1922.

[71] Rühle, R.: Proteins and Bacterial Fermentation, Jahrb. f. Kinderh. **100**: 127 (March) 1923.

[72] Buckheim, I.: Roentgen Examination of Alimentary Tract, Arch. f. Kinderh. **72**:81 (Nov. 18) 1922.

[73] Sauer, L. W.; Minik, L. D., and Alexander, W. G.: Gastric Findings in Children with Anorexia, J. A. M. A. **79**:184 (July 15) 1922.

[74] Kerley, C. G.: New York J. M. **20**:345 (Nov.) 1920; cited by Sauer.

It was found that the stomachs of all twelve children with good appetites emptied within five hours, with an average emptying time of four and one-half hours. For the twenty-one children with poor appetites, the time was six and one-tenth hours.

The average total hydrochloric acid for the children with good appetite was 61.2, the free acid 26.3; for eighteen with poor appetite, the total acid was 49.4, the free acid 14.9.

A relation between these functions and hyposthenia or asthenic habitus was noted. Remedial measures proved helpful.

Chievitz [75] has studied the hydrochloric acid secretion in fifty-three infants after a barley gruel test meal. No instance of congenital achylia was discovered, but there was achylia or hypochylia in almost half the cases of essential digestive disease.

In healthy infants, the values of the free hydrochloric acid averaged 8 (Günzberg), 11 (Congo) and 14 (phenolphthalein).

TETANY

Recent studies on tetany deal chiefly with the blood chemistry of the condition. Freudenberg and György report the successful use clinically of ammonium chlorid.

Elias [76] reminds us that a therapeutic influence of acid or alkali does not prove anything as to the etiology of any disease; in this case, tetany. He maintains that disturbances in the acid-alkali metabolism are not essential for tetany, that the phosphoric acid ion seems to have a special function, in very small doses, of increasing the irritability of the nerves, and that its amount in the blood is increased in tetany.

Hess and Lundagen [77] studied (1921) the phosphate content of the blood of about sixty infants, making monthly examinations by the Bell and Doisy method. The infants were from 6 to 18 months of age, living under good hygienic conditions, and were on a diet of certified raw milk or of dried milk, receiving the usual amount of orange juice, and (the older ones) cereal.

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[75] Chievitz, I.: Hydrochloric Acid in Infants, Acta Pediat. **1**:416 (April 15) 1922; abstr., J. A. M. A. **79**:88 (July 1) 1922.

[76] Elias, H.: Relations of Acid and Alkali to Tetany, Wien. klin. Wchnschr. **35**:784 (Oct. 5) 1922.

[77] Hess, A. F., and Lundagen, M. A.: A Seasonal Tide of Blood Phosphate in Infants, J. A. M. A. **79**:2210 (Dec. 30) 1922.

The plotted findings show a steady seasonal decrease from about 4 mg. in December to a low point (about 3.50 mg.) in March, and then a rapid increase as summer approached (4.50, etc., in June). The phosphate tide was not intimately dependent on the variety of milk fed. The authors are unable to state what the condition may be in breast-fed infants, save that 50 per cent. of well nourished breast-fed infants attending an outpatient department had been found to show clinical evidence of rickets at the end of March, and it seemed probable that they likewise were susceptible to seasonal fluctuations. In older children, the variations were less marked; but in ten children, aged from 2 to 3 years, the rise was definite in every case. In adults, the phosphate content was found to be lower and more stable.

An earlier investigation showed that, in infants, the inorganic phosphates of the blood could be raised to the normal level by frequent exposure of the child to the sun's rays. Later, it was shown that the same result could be accomplished with irradiation with the carbon arc lamp. It seemed probable that the ultraviolet rays were the ones concerned. Comparison of the present curves with meteorologic data for the same period shows a suggestive relationship in the increasing amount of sunshine and daily mean elevation of temperature.

After foreshadowing the existence of a (less marked) seasonal calcium tide, the authors proceed to the generalization that this seasonal variation evidently indicates that the chemical constitution of our blood is not constant for all periods of the year; that this probably holds true for other tissues and that this may exert an influence on general nutrition, growth and resistance to infection.

Greenwald[78] opposes the view that tetany is due to an alkalosis, or increase in the hydroxyl ions in the blood. As tetany following the removal of parathyroids seemed relieved by injections of acid, it was thought an alkalosis existed and was overcome by the acids. This has seemed supported by the fact that tetany has been observed after intravenous administration of alkali, soda bicarbonate solutions, etc. Also gastric tetany has been explained on the assumption that the loss of acid in the gastric juice left a surplus of base in the blood.

According to Greenwald, tetany, instead of being due to alkalosis, is attributable to a high concentration of sodium in the blood. Experimentally produced convulsions are ascribed to "sodium poisoning," a disturbance of the normal equilibrium between sodium and other ions. Even in tetany of hyperpnea, it is not the alkalosis per se but the tissue anoxemia resulting from the increased stability of oxyhemoglobin that is held to be the exciting factor.

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[78] Greenwald, I.: Supposed Relation Between Alkalosis and Tetany, J. Biol. Chem. **54**:285 (Oct.) 1922.

Cruickshank[79] writes that there is a loss of calcium in parathyroid tetany, and that in severe cases the diffusible calcium may amount to 94 per cent. of the total calcium—normally from 60 to 70 per cent.; that the immediate state of alkalosis is not necessarily marked, and with the development of the signs of severe tetany passes rapidly into a condition of acidosis, as shown by a steadily falling p_H of the blood. He adds that the calcium deficiency and the great loss of colloidal calcium are merely indicative of a rapid protein disintegration.

Tisdall and Harris[80] have determined the concentration of phosphorus in forty-five normal persons ranging in ages from 4 months to 44 years, and find that the inorganic phosphate content of normal serum from birth to 20 years is remarkably constant (practically always above 5 mg. per hundred cubic centimeters. At this age, it drops sharply to a lower concentration, and is again remarkably constant at this lower level throughout adult life (below 4 mg. per hundred cubic centimeters.

The drop in phosphate content of the serum at the age of 20 corresponds to the period of cessation of bone-growth. During the period of union of fractures in adults, the phosphate content of the serum is raised to a level approximately the same as that present in childhood; i. e., the period of active bone growth. These findings are presented by the authors in a most striking manner in a graph.

Hamilton,[81] in an extended study on the calcium and phosphorus metabolism of four prematurely born infants, writes that everything tends to show that infants born at term are provided with a surplus of calcium which is lacking in the prematurely born, and found that the calcium intake of his subjects was evidently inadequate to meet their metabolic demands. The author asks whether treatment directed toward correcting an assumed calcium deficit might not ward off rickets and other pathologic conditions common to the prematurely born.

In a clinical case of obstruction of the stomach, in an adult, Grant[82] found the plasma carbon dioxid capacity greatly increased, the blood chlorids markedly decreased and the serum calcium in the upper limits of normal.

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79. Cruickshank, E. W. H.: Experimental Tetany, China M. J. **36**:445 (Nov.) 1922.

80. Tisdall, F. F., and Harris, R. I.: Calcium and Phosphorus Metabolism in Patients with Fractures, J. A. M. A. **79**:884 (Sept. 9) 1922.

81. Hamilton, B.: Metabolism of Prematurely Born Infants, Acta Pediat. **2**:1 (July 31) 1922; abstr., J. A. M. A. **79**:1562 (Oct. 28) 1922.

82. Grant, S. B.: Tetany: Report of Cases with Acid-Base Disturbance, Arch. Int. Med. **30**:355 (Sept.) 1922.

Tisdall,[83] on the other hand, believes the sodium-calcium ratio to be the important factor in the production of tetany, with the exception of the gastric type, in which the disturbance appears due to an increase of the bicarbonate ion. He says no evidence has been found that the calcium-phosphate ratio has any influence on the production of tetany.

On the therapeutic side, Freudenberg and György [84] report that by giving ammonium chlorid from 3 to 7 gm. a day, internally, to spasmophilic infants, they were able to banish the symptoms of tetany and check the mechanical and faradic hyperexcitability. Ammonium chlorid is pleasanter to take than the necessary doses of calcium chlorid (from 6 to 8 gm.) and more acceptable to children. Its effect is only symptomatic, it is said, but immediate danger is averted, and time is gained for employing cod liver oil and quartz lamp irradiation, to bring about permanent change.

THE THYMUS

Hammar [85] presents a lengthy publication on the thymus gland. During his studies over a period of more than twenty years he has investigated the thymus in nearly 300 normal and 500 pathologic cases. He finds that the thymus is never normal after death from disease or in extreme inanition. His microscopic analysis of the thymus in thirty-seven cases of sudden death in children, from internal causes, which might be classed as "thymus deaths," showed that the thymus was of normal size and apparently normal structure in all but five. He finds the thymus is not a transitory organ but functions up to old age. He says the Hassell's corpuscles seem to present the essential functional changes and form the morphologic expression of antitoxic activity. None of the evidence as to an internal secretion from the thymus is conclusive. At puberty, the parenchyma begins to be reduced, but this age involution does not check the antitoxic action of the gland. Roentgen irradiation disintegrates the lymphocytes, and for a time the thymus is changed to a purely epithelial organ.

HEART AND BLOOD VESSELS

Raeder [86] reports an instance of congenital malformation of the heart, associated with anisopia, and with curious branching of the vessels of the aortic arch, occurring in the infant of a primiparous woman, 40

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83. Tisdall, F. F.: Influence of the Sodium Ion in the Production of Tetany, J. Biol. Chem. **54**:35 (Sept.) 1922.

84. Freudenberg and György: Ammonium Chlorid in Tetany, Klin. Wchnschr. **1**:410 (Feb. 25) 1922.

85. Hammar, J. A.: Function of the Thymus, Upsäla Läkaref. Förh. **27**:147 (Aug. 5) 1922.

86. Raeder, O. J.: Congenital Malformation of the Heart, with Complete Obliteration of the Pulmonic Artery, J. A. M. A. **79**:16 (July 1) 1922.

years of age. The presence of small nodules in the valve cusps of the tricuspid valve offered support, as an alternative view to an argument for inflammatory causation (fetal). The anomalies were: complete obliteration of the pulmonary artery at its origin from the right ventricle; perforation of the intraventricular septum; patency of the ductus arteriosus which functioned from birth until death (ninth day); hypertrophy of the right ventricle; presence of an open foramen ovale and of an aortic arch giving origin to a single large branch, which immediately divided into four branches of approximately equal caliber; dilation of the aorta and displacement of its origin to a position almost directly over the malformed intraventricular septum and the presence of small nodules, some of them dark colored, on the mitral and tricuspid valves. The views of various writers on the etiology of such anomalies are given.

An instance of acute infantile endocarditis is described by Skinner.[87] The patient was a 4 months old infant that suffered from an intractable eczema, but otherwise appeared remarkably well. The infant was admitted to the hospital and about fifteen hours later died quietly in his sleep. No symptoms were observed that suggested a cause of death. At necropsy, lesions were found only in the heart and lungs.

On the surfaces of both lungs were several bluish marks about the size of a mustard seed, which on closer examination proved to be minute subpleural hemorrhages. The heart appeared normal in size and color, but the mitral valve was gravely involved, the free edges and auricular surfaces of the cusps being covered with a growth of soft vegetations, not large and quite récent, shining and pink in color and extremely friable. No congenital defects of any kind were present. There was no evidence of pulmonary infarction or cerebral thrombosi. The coronary arteries appeared patent. Skinner thought the most likely explanation of the sudden death lay in the onset of ventricular fibrillation consequent on the presence of an embolus in a coronary artery, sufficiently small to have passed beyond the openings.

Hutchison [88] reports a case of aneurysm of the ductus arteriosus in a girl, aged 6 years, who died from sudden and profuse hemoptysis. The child had not been well since an attack of measles five months earlier, followed by diphtheria and then by "pleurisy." On admission, she complained of pain in the left side of the chest with cough and feverishness. There was a soft systolic murmur at the apex and over the sternum. There was some dulness in the left infraclavicular and suprascapular regions, with diminution of the breath sounds and some crepitation over the right apex in front. The temperature ranged from 100 to 101 F.; the dulness at the left apex became more pronounced as the case progressed, and the apex beat extended further to the left. The short systolic murmur disappeared. Necropsy disclosed a rupture of an aneurysm of the ductus arteriosus into the lung.

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[87] Skinner, E. F.: Case of Infantile Acute Endocarditis, Lancet **1**:1147 (June 10) 1922.

[88] Hutchison, R.: Case of Aneurysm of Ductus Arteriosus, Brit. J. Child. Dis. **19**:85 (April-June) 1922.

An instance of stenosis of the portal vein in a boy of 6 years is reported by Bardach.[89] In early infancy, there had been a suppurative dermatitis with abscesses. At 2 years, there had been a brief period of vomiting of blood, and at 4 years, epistaxis and swelling of the joints. The child had always been pale, and had always refused to eat green vegetables and fruit. Otherwise, he had seemed well.

The presence of a large spleen, severe anemia and profuse hemorrhages in the digestive tract were explained at necropsy as being the result of stenosis of the portal vein. The vein had become imbedded in cicatricial tissue from old peritonitic changes (referable to the suppurative dermatitis of infancy), and stenosed. The splenic vein showed thrombosis, the bleeding came from varices in the digestive tract.

Huber and Koessler,[90] in a study of the pathology of bronchial asthma, state that, even in the purely allergic asthma of a 16-month-old infant (at that age already showing a definite thickening of the bronchial wall, as compared with a well infant of the same age), the exudation into the bronchi and bronchioli, with complete obstruction, is proof of combined action of the exudative and bronchiomuscular systems in the production of stenosis. These observations made it plain to them that, in man at least, the allergic reaction of the tissues is not confined alone to the smooth muscle fiber system, but involves also the whole organ system which serves exudative processes, endothelium, epithelium, capillaries and glands. The paper is well illustrated.

An instance of bilateral cystic kidney in a girl of 3 years, with symptoms of renal insufficiency, dating from 8 months, is reported by Greene.[91] A convulsion at 8 months was perhaps the first of a series of uremic attacks. Albumin was present in the urine throughout the whole period of the disease, and the amount increased during uremic attacks, but was never large. The specific gravity of the urine varied between 1.005 and 1.012; casts were absent and no Bence-Jones or protein body other than serum protein was demonstrable in the urine. Death was due to uremia, with starvation acidosis as a contributing factor.

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[89] Bardach, M.: Stenosis of the Portal Vein in a Child, Arch. f. Kinderh. **71**:*270* (Aug. *26*) *1922*.

[90] Huber, H. L., and Koessler, K. K.: Pathology of Bronchial Asthma, Arch. Int. Med. **30**:689 (Dec.) *1922*.

[91] Greene, C. H.: Bilateral Hypoplastic Cystic Kidneys: Report of a Case Simulating Chronic Diffuse Nephritis, Am. J. Dis. Child. **24**:1 (July) 1922.

The postmortem picture was that of bilateral hypoplasia of the kidneys with cyst formation. The renal tubules were characterized by marked cystlike dilatations, especially on the proximal convoluted tubules. There was no evidence of obstruction, and the dilatation was apparently secondary to functional hypertrophy of the tubules.

An instance of fetal teratoma, the size of an orange, involving the left ovary, in a girl of 6 years and 10 months, is reported by German.[92] He states that the age of the patient is the chief point of interest, as the condition seems to have been reported in only one younger patient (3½ years of age), the next being 11 years old.

In German's case, abdominal symptoms followed a fall over a small rocking chair, and at operation, three weeks later, when there was a leukocyte count of 23,350, an inflamed appendix was found, and a tumor the size of a large orange, blackened and with a twice-twisted pedicle, involving the left ovary. Both were removed. The tumor, a dermoid cyst, contained portions of a fetus, including hairy scalp, a part of the upper jaw, and six teeth, such as those of a 3-year-old child.

Sironi and Sabatini[93] report on a series of twenty cases of enuresis in children. In sixteen, the fifth lumbar vertebra was deformed or there was spina bifida, and in one case, the fifth lumbar vertebra and the sacrum had separated. The authors suggest that such findings indicate that an anatomic basis for enuresis is not rare. They comment on contradictory publications as to malformations, occult spina bifida and the like, as factors in enuresis.

Rivers[94] reports twenty-three new cases of influenza meningitis and reviews the records of 197 other cases. Seventy-nine per cent. of the cases occurred in patients under 2 years of age. The mortality in the 220 cases was 92 per cent. Of the seventeen patients who recovered, twelve were 2 years of age or older.

From the case records, it is possible to say that the meningitis might have been primary in the majority of instances. The disease is produced by a group of influenza bacilli which are closely allied culturally and serologically. Treatments of various kinds have been used, but as far as can be determined, none has accomplished much.

Mackey and Garrod[95] report a case of congenital porphyrinuria and pink teeth, an extremely rare inborn error of metabolism, and give a résumé of the cases previously described. The evidence of congenital onset in their own case, in a 6-year-old boy, is more complete than in other cases. The condition was not familial, and his parents were not blood relatives.

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[92] German, W. H.: Fetal Teratoma in a Child, J. A. M. A. **79**:2000 (Dec. 9) 1922.

[93] Sironi, L., and Sabatini, L.: Essential Enuresis in Children, Riv. di clin. Ped. **20**:399 (July) 1922.

[94] Rivers, T. M.: Influenzal Meningitis, Am. J. Child. Dis. **24**:102 (Aug.) 1922.

[95] Mackey, L., and Garrod, A. E.: Congenital Porphyrinuria, Associated with Hydroa Aestivale and Pink Teeth, Quart. J. Med. **15**:319 (July) 1922.

The boy presented the usual association of porphyrinuria and extreme sensitiveness of the superficial tissues to light, as shown by annual eruptions of hydroa aestivale, or vacciniforme, on the exposed surface of his skin. The deep pink coloration of the milk teeth was quite exceptional. Transillumination of the hands afforded strong evidence that the bones were deeply pigmented, and a roentgenogram showed delayed ossification of the carpal bones.

Halbertsma [96] has found records of nine instances in which one of twins presented mongolian idiocy. He analyses them and reports further five similar instances. The twins were of opposite sexes in all but one instance, and a bivitelline pregnancy may be assumed. In two further cases, the sexes were the same, and both twins were of the mongolian idiot type.

These last two cases sustain the assumption of an endogeneous origin. Halbertsma inclines to incriminate the ovum, as the mothers were mostly close to the extreme end of the reproductive period; in his cases 35, 41, 43 and 44 years old.

DIABETES AND INSULIN

In 1910, Osler, in his textbook, stated that diabetes probably accounted for about ten deaths per hundred thousand population, being apparently about as frequent in the United States as in European countries (8.7 per hundred thousand in England and Wales, and in Paris 14, in 1890). In 1911, Holt stated that the disease was a very infrequent one in children, there being but eight cases in children under 10 years of age in Pavy's collection of 1,360 cases, and only one patient under 10 years of age in Prout's 700 cases. Infrequency of urine examinations in children probably accounts in part for these low figures. Stern collected 117 cases of diabetes in children.

DeLange and Schippers (1915) [97] found between 500 and 600 cases of diabetes in children on record and encountered six cases in 10,848 child patients admitted to one hospital, during eleven years. They reported on eight recent patients, aged 2, 4, 5, 6, 8, 11 and 12 years. Joslin and Gray (1917) [98] analysed a series of 123 cases in patients under 15 years of age; and in a recent report of Joslin's in 127 cases, there were thirty-one under this age. One was 1 year old, and the average age of onset in the thirty-one cases was 7 years.

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[96] 96. Halbertsma, T.: Mongolian Idiocy in Twins, Nederlandsch. Tijdschr. v. Geneesk. **2**:22 (July 1) 1922; abstr., J. A. M. A. **79**:1561 (Oct. 28) 1922.

[97] 97. DeLange, C., and Schippers, J. C.: Diabetes Mellitus in Children, Nederlansch. Tijdschr. v. Geneesk. **2**:785, 1915; abstr., J. A. M. A. **65**:1150 (Sept. 25) 1915.

[98] 98. Joslin, E. P., and Gray, Horace: Diabetes in Children, J. A. M. A. **68**:1869 (June 16) 1917.

Thirst, polyuria and wasting have been the more striking symptoms. Unexplained incontinence may be the earliest symptom noted. Other symptoms are dry mouth, scanty perspiration, irregular sleep, furuncles and abscesses, decayed teeth and genital irritation.

The course has usually been rapid; the younger the child, the more rapid the course. The majority of untreated cases have proved fatal in from two to four months from the time the symptoms became sufficiently marked to make a diagnosis possible; few lasted more than five months, though occasional cases of the milder type lasted a year or two.

In few diseases has the prognosis been so bad as in diabetes of children. Some, as Stern, after a study of seventy-seven cases, have held that diabetes in children is hopeless, and all treatment useless. Holt, in 1911, wrote that he had seen no cases fail to terminate unfavorably. The cases of DeLange and Schippers all terminated fatally in from eight or nine months to two years and a few months. In Joslin's hundred and twenty-three cases, the duration of the disease in patients either living or dead at the time of the report averaged 1.1 years. Five patients had gone on eight or nine years, and appeared to be in good health and sugar-free.

The seat of the disease has been recognized as in the pancreas. The older methods of treatment secured some beneficial results and prolongation of life by keeping the patient's nutritive processes at the lowest possible level by forcing on him food that in a round-about way, rather than in a direct way, was ultimately used by the diseased pancreas. Whether anything in the nature of a cure of the disease has ever been approached may well be doubted.

With the discovery of insulin, a new chapter in the history and treatment of diabetes is opened. Ever since Mering and Minkowsky, by surgical experiments on dogs, demonstrated the existence of pancreatic diabetes, attempts at specific pancreatic therapy have been made, but have been uniformly unsuccessful, and are now chiefly of historical interest. It was reserved for Banting and his co-workers, in 1921, to isolate an active, glycolytic, nontoxic pancreatic extract, called by them insulin.

Allen [99] has written an excellent summary of the articles published on this subject up to 1922, presenting the various steps in developing Banting's important discovery. A more recent article by Banting and

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99. Allen, F. M.: Summary of Publications on Insulin to Date, J. Metabolic Res. **2**:125 (July) 1922.

others [100] describes the clinical results obtained in diabetics. The insulin which is made in the United States (Iletin-Lilly) has been used extensively in this country during the last few months.

Major [101] describes a case of severe juvenile diabetes. His first photograph (taken Dec. 7, 1922) shows the patient when he had been a diabetic for two years, and it had been impossible to render him aglycosuric except on a diet of 5 per cent. vegetables, with days of complete starvation. His weight had fallen to 18 pounds (8.2 kg.). A second photograph, taken Feb. 26, 1923, after the patient had been under treatment a little over two months, shows him weighing 30 pounds (13.6 kg.) and on a diet containing 55 gm. of carbohydrate, 85 gm. of protein, and 100 gm. of fat. April 15, the child was in excellent condition, weighed 32 pounds (14.5 kg.), and was receiving a diet consisting of 60 gm. of carbohydrate, 80 gm. of protein and 70 gm. of fat.

During a period of three months, the daily dosage of insulin was reduced from 75 to 15 units. This, Major felt, was indication of an increasing tolerance.

Insulin is described as an aqueous solution of an active principle from the pancreas, which affects sugar metabolism. Its administration to man in severe cases of diabetes restores to the body the lost ability to oxidize carbohydrate, and glycogen is again stored in the liver. If the solution is administered (hypodermically) at suitable intervals, the blood sugar is maintained at a normal level, and the urine remains free from sugar. Fat is also burned and, as a result, ketone bodies do not appear in the urine, and diabetic acidosis and coma are averted.

The use of insulin greatly simplifies the diet of diabetic patients. Enough carbohydrate can always be ingested and utilized to supply the normal carbohydrate demand for the complete and proper metabolism of the other food principles desired by the patient (Cowie and Parsons), provided, of course, the demand is not excessive. It permits giving a diet that satisfies the natural, normal cravings of the patient; permits of maintaining a more comfortable weight, and improves the patient's mental attitude.

Yet it is not to be forgotten that the substance is a powerful drug, and an overdose is followed by the development of serious symptoms which demand immediate treatment. If insulin is to be administered without adequate control of the blood sugar, it is safer to have the blood sugar somewhat above normal, with transient glycosuria, than to have the urine sugar-free and the blood sugar at or below normal.

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100. Banting, F. G.; Campbell, W. R., and Fletcher, A. A.: Further Clinical Experiences with Insulin, Brit. M. J. **1**:8 (Jan. 6) 1923.

101. Major, R. N.: The Treatment of Diabetes Mellitus with Insulin, J. A. M. A. **80**:1597 (June 2) 1923.

In babies, it would seem that less danger attends the administration of insulin because the usual method of spacing feedings can be taken advantage of to insure sufficient carbohydrate coming into the blood stream at a time when otherwise the effect of the dose (hyperinsulemia) might cause a dangerous reduction of the blood sugar.

In children who are no longer bottle-fed, danger might easily arise because of the inability of the child to announce developing symptoms. Careful management and suitable spacing of the meals is necessary.

It is to be remembered that insulin is not yet advanced as a cure for diabetes; it is one more means of treatment. All the other means are to be conserved, utilized. The administration of insulin will enable the patient to have carbohydrate so that protein and fat can be added to the diet in sufficient quantities to give him energy to carry on work and to maintain the ordinary economic burdens of life. His diet is rendered appetizing, and life is made more tolerable. It is possible also that the improved general health and the lightening of the burden of work to be borne by the diseased organ may result in regenerative processes setting in.

Whether insulin is to be regarded as by any means a cure for diabetes in children remains to be seen. In some patients, progressively smaller doses of insulin are needed to take care of the excess of sugar in the blood. It may well be that, in time, some of the patients will improve to such an extent as to be able to get along without the drug, and eventually can eat ordinary diet without glycosuria. They may perhaps then be said to be cured.

The interesting point has been made [102] that if the administration of insulin increases the expectation of life (of diabetics) to that of non-diabetics, it will not be long before there will be a greatly increased number of diabetics in the population. This will increase the need for the drug. Collip [103] has recently obtained a substance somewhat similar to insulin from various plants.

Charles Street at Thirty-Fourth.

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102. "W. S. T.": Clifton M. Bull. **9**:41 (June) 1923.
103. Collip, T. B.: Proc. Soc. Exper. Biol. & Med. **22**:321.

BOOK REVIEW

LE DISPENSAIRE MARIN. UN ORGANISME NOUVEAU DE PUERICULTURE. By J. Jarricot, Paris, Masson and Company, 1921.

This rather bulky volume does not carry conviction. The use of sea water in the treatment of infants may be excellent, but we do not feel that the author has proved his point. In discussing his cases, the author does not seem to have used true standards for comparison and, therefore, his conclusions are of doubtful value. For example, he compares the rate of growth of a sick infant, under sea water therapy, with the rate of growth of a normal child of the same age, instead of comparing it with the growth of similar sick infants who had no treatment or who had other standard forms of therapy.

The author repeats himself often, and the book is filled with much extraneous material.

American Journal of Diseases of Children

VOL. 27 APRIL, 1924 No. 4

STUDIES ON ANEMIA IN INFANCY: THE UROBILIN CONTENT OF THE STOOLS OF NORMAL INFANTS *

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During the past decade the problem of the anemias has been approached by new paths. Interest centers not so much in the morphology as in the physiology of the blood, the way the hematopoietic system performs its function. The function of the blood forming organs is to preserve the hemoglobin, and the red and white cells at a certain level. This stability is maintained by a balance between two opposing forces; the continuous destruction of blood cells is compensated by an equivalent regeneration.

There is no single criterion of blood regeneration. When the percentage of hemoglobin, and the number of red and white cells fall within normal limits, and there are no abnormal cells in the blood stream, blood regeneration may be considered normal. The presence in the circulation of immature cells reflects the degree of strain under which the bone marrow is working. Nucleated forms, normoblasts and megaloblasts, indicate a severe functional incapacity. An excessive number of reticulated cells indicates a lesser degree of injury. Reticulated cells are non-nucleated red cells that show a fine black skein or reticulum, or only black granulations, when vitally stained by such dyes as cresyl blue. In normal adult blood they form about 0.5 per cent. of the red cells and in the blood of infants a somewhat higher percentage. Though still immature, they are more nearly completely developed than are the nucleated red cells. Their presence in excess indicates that the bone marrow is responding well to demands made on it by the production of cells closely approaching normal. Thus, one function of the blood forming organs, blood regeneration,

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* Received for publication, Jan. 21, 1924.

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may be gauged by the number of red and white cells, the percentage of hemoglobin and the presence and number of immature and abnormal forms.[1]

To determine the degree of blood destruction we have relied on the estimation of the amount of urobilin and urobilinogen in the feces. The association of urobilin with the fate of hemoglobin is illustrated in Table 1. This conception in its entirety is not universally accepted.

Table 1.—*The Association of Urobilinogen with the Fate of Hemoglobin*

Liver		Bile Passages	Intestine	Portal Stream	Liver
			part destroyed		
Hemoglobin-Hemochromogen——		Bilirubin—	Urobilin———	Urobilin—	Bilirubin-Hemoglobin?
Globin	Iron salt		*part excreted		

* Only this portion of the urobilin, the amount excreted in the feces, can be estimated.

According to Whipple, urobilin may be synthesized by the liver cells and Whipple also questions the reabsorption of bile pigments from the intestine, the classical theory of "the circulation of the bile." [2] In addition, adventitious circumstances, mentioned under technic, affect the quantitative accuracy of the method of estimating urobilin devised by Wilbur and Addis and used in the present work. Nevertheless, urobilin estimation is a sufficiently accurate indicator of the degree of blood destruction for clinical work.

The final purpose of this work is to determine the rôle of excessive blood destruction in certain of the anemias of infancy. Possibly the anemias of infancy might fall naturally into certain groups, depending on whether there is excessive blood destruction, inadequate regeneration or both. Preliminary to such studies it was necessary to determine the urobilin output in the stools of normal infants, or rather of infants whose hemoglobin fell within normal limits, and who were not suffering from any acute disease.

Normal hemoglobin values are subject to wide variations in infancy. Williamson [3] demonstrated this in very striking manner by the estimation of the hemoglobin of normal individuals with the spectrophotometer. The chart, taken from his work, presents the hemoglobin values for children under 4 years of age. The variation depending on age is extreme. The average drops from 21 gm. per hundred cubic centimeters of blood, at 2 weeks, to 13 gm. at 3 months of age. The variation among individuals of the same age group is still greater. In the chart, the middle line indicates the average of all the infants examined; the two other lines indicate the average of all those above and below the general average. From the sixth to the twelfth month the upper and lower limits of normal range from 10.8 to 14.2 gm. per hundred cubic centimeters. Or, to express this in the usual terminology, in the percentage of hemoglobin the normal variation ranges from 72 per cent. to 95 per cent.[4] Evidently, decision as to the presence and degree of

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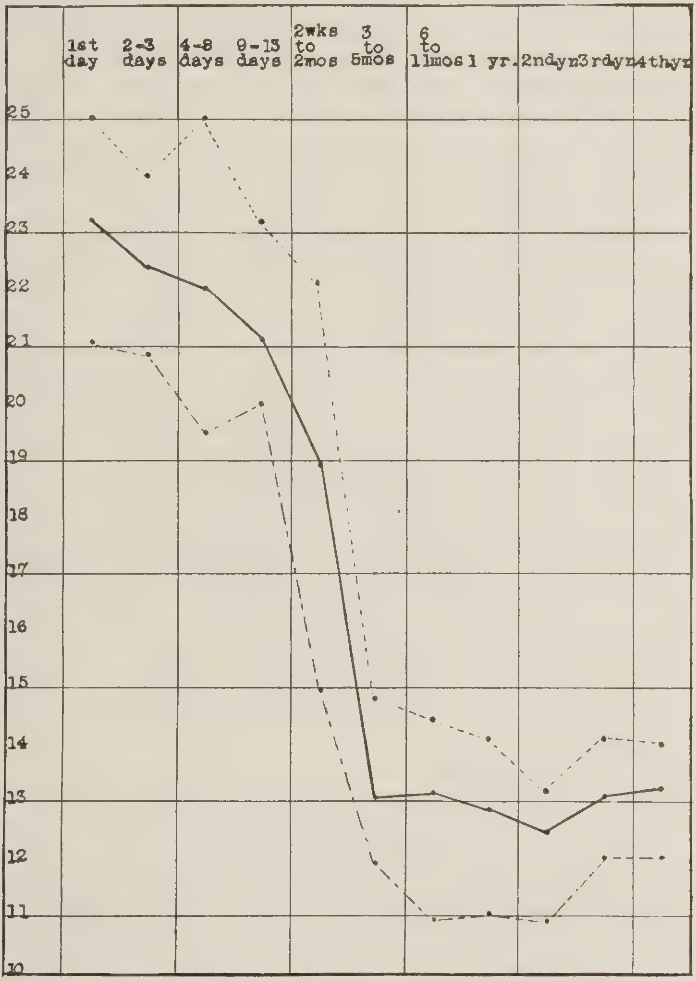
[1] There are other criteria of blood regeneration. Hurwitz, in Metabolism and Endocrinology, Vol. 4, New York, D. Appleton & Company, 1922, presents a brief and very clear account of the physiology of the hematopoietic system.

[2] Hooper, C. W., and Whipple, G. H.: Am. J. Physiol. **42**:764, 1916-1917; ibid, J. Exper. Med. **17**:612, 1913.

[3] Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18**:505 (Oct.) 1916.



Grams of hemoglobin per hundred cubic centimeters in normal children.

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[4] According to the standard used by us, 15 gm. per hundred cubic centimeters equals 100 per cent.

anemia must take into consideration, first, the variation dependent on age, and secondly, the individual variation within the age group.

With the exception of the infants that were only a few weeks of age, our cases were drawn from the "Feeding Ward" of the pediatric service of the New York Nursery and Child's Hospital. Few of the babies were vigorous and perfectly healthy; many were illnourished and underweight and a few suffered from slight ailments such as otitis, nasopharyngitis, mild impetigo, etc. All showed hemoglobin values above the lower limit of normal. As might be expected from their general condition, most of the hemoglobin percentages hovered about the lower rather than the upper limit of normal.

Hemoglobin determinations were made with Kuttner-Leitz hemoglobinometer.[5]

The method used for the determination of urobilin in the feces is that of Wilbur and Addis.[6] Certain modifications (the fact that we were working with infants' stools and used a different spectroscope) necessitate a description of the technic. Essentially, the method consists in the extraction of the feces and the addition of Ehrlich's reagent to the extract to produce the characteristic spectroscopic absorption bands of urobilin and urobilinogen. The quantity of the pigments is expressed by the number of dilutions necessary to cause the disappearance of the bands. The proportion of the two substances varies considerably and only the sum of their dilution values is of clinical significance; and hereafter the term urobilin without the mention of urobilinogen will refer to the combined value of the two. The daily variation in the excretion of urobilin is very great, and to minimize this variation repeated stool examinations are necessary. In all but a few of our cases the stools of our patients were examined for a period of six successive days. When spontaneous evacuation failed to occur, suppositories were used.[7]

Technic.—The soiled diapers were placed in metal cans immediately on their removal, to protect them from the light. All of the stool passed in the twenty-four hour period was used for the test. The feces were scraped from the diaper with a spatula and ground with tap water, just enough water being used to make a smooth suspension. When no urobilin at all or only a small amount was found, a more concentrated suspension was made on succeeding days. The stool suspensions varied from 25 c.c., the smallest amount that can be used, to 200 c.c. To 25 c.c. of this suspension were added 75 c.c. of acid alcohol (95 per cent. alcohol 1,600 c.c., concentrated hydrochloric acid 25 c.c., and water 800 c.c.), and the mixture was shaken thoroughly for thirty minutes. With this, an equal quantity (100 c.c.) of a saturated solution of zinc acetate in alcohol was mixed and shaken for a moment before filtering. To 20 c.c. of the filtrate, 2 c.c. of Ehrlich's reagent was added.[8] This was put aside in a dark place until the following day, when spectroscopic examination was made. The urobilinogen band is extremely sharp and lies between the red and the yellow. The urobilin band is not so distinct and lies between the yellow and the blue. Daylight or a Daylo lamp was used. The solution was diluted with 60 per cent. alcohol until first one and then the other band had disappeared.[9] The lowest dilution at which the band was still visible was considered the final reaction. The method of calculation was as follows: 25 c.c. of stool suspension plus 75 c.c. alcohol and 100 c.c. of zinc acetate in alcohol equals 200 c.c. Twenty cubic centimeters of this, or in other words, the extract of 2.5 c.c. of stool suspension was mixed with Ehrlich's reagent and used for the test. Thus the dilution required to cause the disappearance of the band gave the dilution value for 2.5 c.c. of stool suspension. If this figure is multiplied by the number of 2.5 c.c. quantities in the stool suspension, the number of dilutions is obtained that would be necessary if all the urobilin or urobilinogen were concentrated in the 2.5 c.c. of stool suspension. For instance, assume that a 100 c.c. stool suspension had been made. The urobilinogen band has disappeared after ten dilutions. There are forty 2.5 c.c. quantities in 100 c.c. Then forty times ten, or 400, equals the dilution value for urobilinogen. The urobilin band disappeared after five dilutions. Then forty times five, or 200, equals the urobilin dilution. The dilution value for total urobilin is 400 plus 200, or 600.

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[5] We are indebted to Dr. Soma Weiss for the standardization of the apparatus.

[6] Wilbur, R. L., and Addis, Thomas: Urobilin: Its Clinical Significance, Arch. Int. Med. **13**:235-286 (Feb.) 1914.

[7] In the original article of Wilbur and Addis a full discussion will be found of the relation of urobilinogen and urobilin to one another, the effect of constipation and diarrhea on urobilin excretion and the limitations of the test as a quantitative method.

Table 2 summarizes the dilution values in the stools of sixteen infants under 1 year of age. Urobilin was found as early as the second week. Lucas[10] and his collaborators, who used the method of Wilbur and Addis, failed to find urobilin in the stools of infants under 10 weeks of age. Our technic differed in that more concentrated suspensions of feces were used, and this may account for the divergent results. In considering the wide variation in the amount of urobilin, the factors governing its excretion must be given due weight. Some and probably variable amounts may be reabsorbed; some also is destroyed in the intestines (Table 1). The amount also is influenced by the rate at which the feces pass through the intestinal canal; diarrhea increases and constipation diminishes the output. We do not know whether the kind of food and the nutritional condition of the infant are also factors. The variation is hardly more than to be expected, considering the wide variation in the urobilin excretion of normal adults, in whom Wilbur and Addis found values varying from 3,000 to 8,000.

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[8] Paradimethylamidobenzaldehyde 4 gm., concentrated hydrochloric acid 30 gm., water 30 gm.

[9] Wilbur and Addis recommend a spectroscope with an attachment to control the light. They consider the end reaction to be that dilution at which the band is visible when the slit is narrowed and disappears when the slit is open. When we began our work, only a simple spectroscope without an adjustable slit was available. Recently we have used a finer instrument with an adjustable slit which is far more accurate and satisfactory.

[10] Lucas, W. P., et al.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

Table 2.—*The Dilution Values in the Stools of Sixteen Infants Under 1 Year*

Case	Period of Observation, Days	Age	Weight, Pounds	Hemoglobin, Gm. per Hundred C.c.	Average Total Urobilin Values
1	6	3d to 10th day	6 4/16	20.5	0
2	7	5th to 15th day	5 14/16	18.1	15
3	8	3 weeks	6 2/16	18.1	10
4	8	4 weeks	9 8/16	14	53
5	6	6 weeks	6 8/16	13.1	109
6	7	9 weeks	7 10/16	11.5	30
7	7	3½ months	7	11.5	59
8	6	4 months	8 8/16	12.3	83
9	6	4½ months	11 4/16	12.6	119
10	6	5 months	10	13.1	40
11	7	6½ months	8	12.6	21
12	8	7 months	11 10/16	11.1	86
13	6	8 months	16	10.7	117
14	4	8 months	15 14/16	12.3	62
15	8	9 months	15	10.8	60
16	6	11 months	12 4/16	11.2	24

SUMMARY

1. The present conception that the status of the hemoglobin and formed elements of the blood is the result of a balance between blood destruction and regeneration, suggests the study of some of the anemias of infancy from that point of view.

2. The estimation of the degree of anemia must take into consideration the wide normal variations in the hemoglobin.

3. Urobilin is found in the stools of infants as early as the second week.

4. The urobilin of the stools of normal infants from 2 weeks to 1 year of age varies from fifteen to one hundred and fifty dilution units, according to the method of Wilbur and Addis.

MENINGEAL HEMORRHAGES IN THE NEW-BORN AND THEIR REMOTE CONSEQUENCES *

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From the onset of embryonic life up to the period of birth, the fetus is exposed to multiple damaging influences having a direct bearing on the growth of the central nervous system. Lesions of the latter may be numerous, and vary with regard to their localizations, extent and depth. They are apt to compromise the cerebral functions not only at the time the damage is done but especially during later development of the nervous system. If the infant survives, infirmities are seen not only in the sensorimotor sphere but also and more particularly in the mental faculties in which a definite defect is manifest. Of the many facts that are likely to lead to such consequences, only meningeal hemorrhages at birth will be discussed here.

During birth, hemorrhages may occur at different levels, either within the nervous tissue itself or close to the cranium. In the latter case, the blood may be located between the bone and its periosteum (cephalhematoma); between the periosteum and the dura, or beneath the dura.

In order to understand the mechanism of formation of hemorrhagic foci, a brief account of the anatomic arrangement of the membranes with their vascular supply is necessary.

The dura mater consists of two layers, an inner and an outer one. The outer, which is the periosteal membrane, sends septums into the cranial cavity accompanied by venous sinuses. These sinuses are the falx cerebri, which encloses the superior and inferior sagittal sinuses, also the straight sinus along the line of junction of the base of the falx with the tentorium; the tentorium cerebelli with the transverse and superior petrosal sinuses, and the falx cerebelli with the occipital sinus. The septums are reinforced in certain places by an aggregation of fibrous bands which enable the head to withstand the great strain in accouchement.

During a difficult labor, the frequent changes in the shape of the head and the excessive tension overstretch the septums, and tears follow. These tears may be complete or incomplete, unilateral or bilateral. When the tentorium cerebelli is involved, the tear is usually found below its junction with the falx cerebelli. When the falx cerebri is damaged, the

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* Received for publication, Nov. 28, 1923.

* Read by invitation before the Obstetrical Society of Philadelphia, Oct. 12, 1923.

tear occurs at the level of its middle two thirds. Holland [1] found in a series of 167 cases tears in the tentorium in 48 per cent., and in all of the latter, subdural hemorrhages. The fine blood vessels and the large vein on the border of the small circumference of the tentorium are the sources of hemorrhages. The usual origin of hemorrhages is in the tributaries of Galen's vein received from the cerebellum and midbrain, and from the cerebellar veins entering the straight sinus. The experimental investigations of Holland prove this contention conclusively. These tributary veins are stretched between the fixed point of Galen's vein and the fixed cerebellum. During the excessvie tension in difficult labor the apex of the tentorium is drawn upward, and consequently the Galen's vein is twisted at its entrance into the sinus. An enormous distention of this vein and of its tributaries follows. On the other hand, the cerebellum is at that time pressed down into the posterior fossa by the undue pressure of the occipital lobes of the brain. Under such circumstances, the fine vein tributaries of Galen's vein, as well as the cerebellar veins entering the straight sinus, rupture.

Over the surface of the cerebral hemisphere, similar subdural hemorrhages may occur during difficult labor, and they are particularly intense in a foot presentation. They commonly occur between the layers of the falx cerebri, although less frequently than in cases involving the tentorium. Occasionally there may be a hemorrhage at the base of the brain. Rarely does the pia-arachnoid tear, but in such cases small hematomas occur.

Ventricular hemorrhages, although rare, may occur from extreme extension of the fine veins of the choroid plexuses.

The seat of hemorrhages is of importance. In the cases involving the tentorium, for example, even a small blood effusion beneath the tentorium would be of graver consequence than one on its surface however large it might be. Tears in the tentorium cerebelli are the most common occurrence. Those of the falx cerebri are next in frequency and are rather rare. In the majority of cases, they are associated with tears in the tentorium.

In considering the causes of meningeal hemorrhages, it is extremely important to bear in mind the immediate and the predisposing factors. Infections and intoxications in utero may be the direct cause, but the most frequent one is traumatism during the confinement, namely, extraction of the head last, forceps delivery from contracted pelvis or presentation of the face or of the forehead. As to breech presentation statistics show that tearing of the tentorium was found in about from 70 to 75 per cent. of dead fetuses thus delivered. Holland believes that in such cases the condition of the tentorium was due to the endeavor to effect a rapid delivery after version; but if breech delivery is properly managed, there should not be sufficient intracranial tension to produce tearing of the tentorium. The same view can be applied to the cases with transverse presentation. Circulatory interference in the umbilical cord and congenital malformations of the central nervous system are also frequently the cause of intracranial hemorrhages.

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[1] Holland, E.: Report on the Causation of Foetal Death, London, Reports on Public Health, 1922.

The frequency of meningeal hemorrhages in the new-born may be seen from the statistics of Hedrén [2] of Stockholm, and Cruickshank.[3] The former examined 700 cadavers of infants and found intracranial hemorrhages in about 9.28 per cent. The bleeding was restricted to the meninges in nearly 84 per cent., and cerebral hemorrhage, accompanied by meningeal hemorrhage in others, brings the total of meningeal hemorrhages to 90.7 per cent. Delivery had been spontaneous in fifty of the sixty-five cases, and the conditions in both mother and child seemed to be normal in most of the cases. In the forty-two purely meningeal cases, the hemorrhage had been supratentorial in thirty-two, infratentorial in ten and of both types in six. An analysis of these cases leads to the conclusion that intracranial hemorrhages may occur with rapid and easy spontaneous delivery and they may occur without fracture of bone.

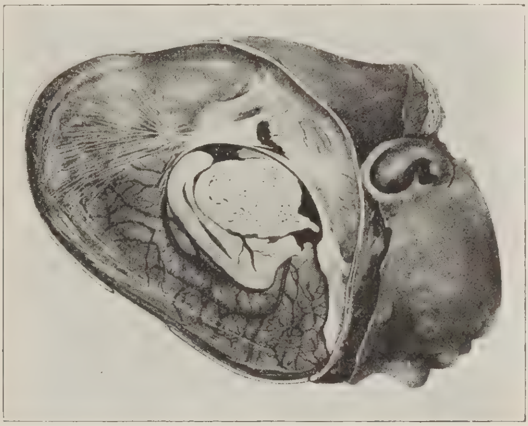

Fig. 1.—Incomplete tear of tentorium cerebelli on right side; the tear is across the fibers at the base of the anterior vertical band. The head shows extreme molding, after labor with generally contracted pelvis. Note elevation of apex of tentorium and change in direction of Galen's vein and straight sinus (Holland).

In Cruickshank's account of 200 cases, one finds the incidence of sixty-five cases which showed meningeal hemorrhages of a gross character. In twenty-five cases there was meningeal hemorrhage associated with hemorrhage into the viscera.

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[2] Hedrén, G.: Intracranial Hemorrhage in the New-Born, Abstr. J. A. M. A. **70**:1988 (June 22) 1918.

[3] Cruickshank, J. W.: Lancet. **1**:836 (April 28) 1923.

CLINICAL MANIFESTATIONS

Meningeal hemorrhage is more frequently suspected than actually determined during life. Death may ensue in a few hours following the meningeal hemorrhage, but if the infant survives, a state of apparent collapse is observed, cyanosis, low temperature, convulsions on subsequent days, circulatory and respiratory disturbances, various palsies and contractures. When the infant further succeeds in overcoming the immediate effect of the bleeding, the above mentioned stormy symptoms gradually subside and the child enters into a chronic state of physical and mental inferiority with a crippled central nervous system. Diplegia, hemiplegia, spastic paraplegia, contractures, athetosic or choreiform movements, convulsive phenomena, amaurosis, mental deficiency or debility of various degrees—all form a symptom group which could be placed under one caption of infantile encephalopathies. Of course, this vast group presents various degrees in its extent and intensity. There are mild cases and cases in which the damage is profound. From the standpoint of intellectual development, the child may be an idiot or an imbecile, or may present only a slight degree of mentally arrested development. It all depends on the hemorrhage and on the facility with which the blood may be absorbed or otherwise removed.

The encephalopathies may be early or precociously diffuse, which will lead to idiocy; they may be late or delayed, circumscribed and frequently slight, which in adult life will be manifested in but slight disturbances of intelligence. The arrest of intellectual development will be especially pronounced and less amenable to improvement in those cases which, through hereditary factors, are inevitably predisposed to and prepared for disturbances or anomalies of cerebration.

A brief physiologic consideration is warranted. At birth, the cells of the central nervous system are fully developed. As to the nerve fibers, full growth is present only in those which control reflex movements, circulation, respiration and nutrition, in other words, the nervous mechanism of the spinal cord and medulla alone are functioning at that period of life. On the other hand, the fibers originating in the frontal, rolandic, occipital, parietal and temporal regions of the brain, as well as the projection and commissural fibers, become myelinated only some time after birth. It is evident, therefore, that early symptoms will be only those which are in relation to the physiologic function of the medulla and spinal cord, but manifestations depending on the function of various portions of the brain will be in evidence ulteriorly and for the above mentioned reasons will remain permanent. If we add to them the compression of the convolutions caused by the blood, also the possibility of the breaking up of the cerebral tissue and infiltration of the latter with the blood, the physiologic damage is easily conceived.

A brief description of the several clinical varieties may be helpful for a full understanding of hemorrhagic possibilities.

CEREBRAL DIPLEGIA

Two important subvarieties should be considered. One is the classic Little's disease, in which there is a spastic paraplegia of the upper and lower extremities, and in which the spasticity is more pronounced than the paralysis but there are no convulsive phenomena and the intelligence is preserved. Improvement is a common occurrence. This form is fundamentally of agenesic order and due to a congenital insufficiency of the pyramidal tract. Premature birth is the original cause.

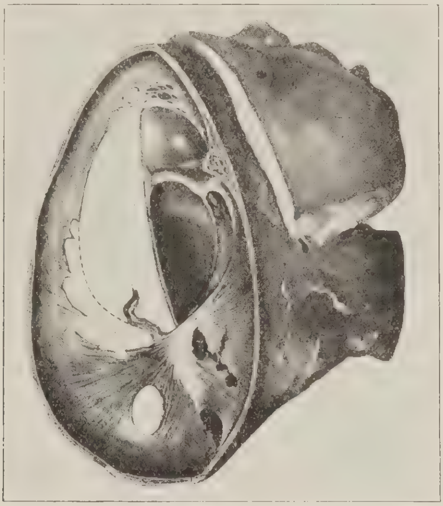

Fig. 2.—Complete tear of tentorium and extensive tearing of falx. In the tentorium there are two perforating tears on left side; one is a ragged tear starting below the base of the anterior vertical band and extending outward almost to the lateral border of tentorium. The other is a large perforation through the superior wall of the left lateral sinus at its termination in the torcular herophili (Holland).

The second variety is due to destructive lesions of an inflammatory or traumatic origin, of a toxi-infectious or obstetric cause, namely, a difficult delivery producing tears in membranous blood vessels of the brain. Here the motor areas, as well as other portions of the cortex, are usually involved, spasticity and paralysis being produced, as well as serious convulsive phenomena and disturbance of intelligence. The condition is persistent, and is permanent. The clinical picture of the last form of cerebral diplegia will vary according to the predominance of involvement of different areas. The association of intellectual phenomena with paralysis and spasticity of the limbs indicates a lesion in the frontal and rolandic areas. Here one or the other may predominate, but the presence of epileptiform manifestations is always an unfavorable condition for the intellectual development, and in all such cases the mental deficit is pronounced. Athetosic and choreic movements are also frequently observed in this variety of diplegia.

An interesting feature of the intellectual status in the first variety of diplegia deserves special mention. There is a striking discord between the appearance of the little patients and the real state of intelligence. At first glance, the difficult speech and the expression of the face with the mouth open may suggest a low mental state, but an actual test and close observation of their behavior and of their relation to the environment will reveal an integrity of intelligence.

The difference, consequently, between the two forms of diplegia is fundamental, and its second variety is far more serious than the first. Since it is due to obstetric traumas, the value of meningeal hemorrhages in difficult labor cannot be overestimated.

CEREBRAL HEMIPLEGIA

Should the hemorrhage be limited to one hemisphere, hemiplegia with all its characteristics will be the result. In almost all such cases, there is an intellectual deficit, more or less pronounced; all degrees between ordinary mental arrest and idiocy are observed. The inequality and irregularity in the intellectual deficit is due to the great variation in the extent and intensity of the lesions in one hemisphere. As to the hemiplegia itself, it differs from the same occurrence in an adult because, in addition to the paralysis there is considerable lack of development of the affected limbs: they are small not only as regards musculature but also bony tissue; there are permanent contractures with secondary deformities, hemiathetosic and hemichoreic movements; also, frequently, aphasia is absent in cases of right hemiplegia.

Frequently with, and in place of, complete or incomplete intellectual obliteration, other spheres of sensory psychic activity are developed, but close analysis will reveal that the latter are only of a purely reflex character, are automatic and lack in associative integration, and therefore lose all psychic value.

DOUBLE ATHETOSIS AND ATHETCSO-CHOREIC MOVEMENTS

As is shown in the foregoing, encephalopathies in infants may be manifested by a more or less marked deficit in the intellectual sphere, and accompanied by bilateral motor phenomena in the form of chorea or athetosis. Again, various degrees of involvement may be present: there are cases with very slight disturbances in the psychic sphere, in which, on the contrary, the motor manifestations are most conspicuous. There are cases in which the two conditions are reversed. They are all observed in infants that were born by instrumental delivery, and consequently sustained traumas and suffered from meningeal hemorrhages during birth.

The three forms of encephalopathies described are the extreme and gross types. There are many intermediary forms which depend on the portion of the brain affected by the meningeal hemorrhage. Thus, any portion of the rolandic area may be affected: the centers of the leg or arm, face, lips or tongue may be individually compressed. There are cases with a minimum of diplegia; with pseudobulbar manifestations; with speech defects showing involvement of the speech centers, motor or sensory; with an exclusive mental defect indicating an involvement of the frontal lobes; with persistent and frequent epileptiform convulsions in which, particularly, the mental development suffers the most. Finally, there may be cases with unilateral or bilateral cerebellar manifestations, the so-called cerebellar hemiplegia or diplegia types, in which cerebellar manifestations alone are conspicuous.

CONCLUSIONS

The cause of meningeal hemorrhages is, principally, the tearing of the membranes due to their overstretching, which leads to rupture of the blood vessels. To produce a tear, there must be great cranial stress. Since the latter is frequently the result of protracted, difficult labor, with instrumental delivery, the obstetrician should bear in mind that the force used in the application of forceps should not be excessive, or should not be applied to the wrong diameter of the head, as, for example, the anteroposterior diameter. In the latter case, the vertical elongation of the head is, more than anything else, liable to cause overstretching and tearing of the meninges. Forceps are useful, and in many instances have been responsible for saving lives, but they may also be responsible for injuries in the fetus leading to consequences which have a direct bearing on the later physical and mental development of the child.

The preventive aspect lies in the consideration of all forces that are liable to lead to tearing of the meninges and the blood vessels. Wrong presentation and position of the fetus and other causes of difficult labor, such as prolapse of umbilical cord, the use of instruments or various manipulations in the delivery of the fetus, are all factors that cannot be overestimated in the production of cerebral hemorrhages and the tearing of the meninges.

Besides the preventive phase, let us consider briefly the therapeutic aspect of meningeal hemorrhage. With a certain degree of possible errors, supratentorial hemorrhages, generally speaking, present a somewhat different clinical picture from the infratentiorial type. In the former, the blood spreads over the hemispheres of the cerebrum; in the latter, over the hemispheres of the cerebellum but also into the medulla. In the former, the blood cannot go beyond the lower surface of the tentorium; in the latter, the blood reaches the subarachnoid space and may extend into the spinal canal.

For these reasons, in the supratentorial hemorrhage at birth one finds a bulging fontanel and a group of nervous phenomena, such as sleeplessness and great restlessness and convulsive seizures, with a continuation of the condition. In infratentorial hemorrhage, there is considerable depression, apathy, somnolence, early cyanosis, vasomotor and respiratory manifestations and rigidity of the neck muscles. In view of the anatomic differences, respiratory and other bulbar disturbances will not be observed in the cases of supratentorial hemorrhage.

Cyanosis is late in appearing and, when it does appear, is not pronounced in the supratentorial hemorrhages, but is early and very pronounced in the infratentorial cases; the anterior fontanel is at once bulging and early in appearance in the supratentorial, but slowly distending in the infratentorial cases.

For anatomic reasons, in infratentorial cases lumbar puncture may be of considerable benefit. Advocated first by Devraigne,[4] it was rapidly adopted by others, and favorable or very satisfactory results have been reported in the literature. Frequently, the withdrawal of spinal fluid needs to be repeated. In some cases, such as that of Lippman, one puncture may suffice. His patient presented convulsions, cyanosis, and frigidity. As the convulsions increased in intensity, Lippman [5] removed 25 c.c. of bloody spinal fluid. Complete recovery followed. In Green's [6] case, there were convulsions, cyanosis and apnea. Four punctures were made, 5 c.c. of bloody spinal fluid being removed each time, and all the symptoms disappeared. Brady [7] recently report very favorable results from lumbar punctures and removal of some spinal fluid. In the supratentorial cases lumbar puncture does not avail much, as the blood cannot reach the subarachnoid cavity easily. Surgical therapy is almost the only issue. Early craniotomy is directly indicated. Favorable results from the very nature of the condition can be expected only when an operation is performed within a few days after birth. After

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4. Devraigne: Thèse de Paris de Dutreix, 1905.

5. Lippman, U. J.: New York M. J. **103**:263 (Feb. 5) 1916.

6. Green, R. M.: Bost. M. & S. J. **174**:947 (June 29) 1916.

7. Brady, J. U.: Lumbar Puncture in Meningeal Hemorrhage of the New-Born, J. A. M. A. **71**:347 (Aug. 3) 1918.

the clot has already produced damage to the cortical tissue, no relief can be expected. Cushing,[8] who obtained four complete recoveries in nine cases, is of the opinion that no hesitation should exist in operating on such young infants, in view of the fact that the new-born can withstand cranial operations better than any other operation and that much less traumatism is created by an operation than by the passage of the head through the pelvis during birth. With proper hemostasis and proper preservation of the body temperature during the operation, the possibility of surgical success, Cushing claims, is secured. In his fatal cases, he found extensive extravasation over entire hemispheres, and the patients were in a dying condition. Not too much, he counsels, should be attempted at one sitting, and a secondary intervention is advisable.

Henschen [9] advised aspiration of the cranial subdural space in supratentorial cases, followed by an incision through the coronal suture. Brady suggests in supratentorial cases, first a lumbar puncture, and immediately afterward incision below the parietal suture. It seems logical that in all cases indicating increased intracranial pressure at birth, lumbar puncture should be resorted to at once, before a definite localizing diagnosis is made, since in the infratentorial group it is of definite therapeutic value, and in the supratentorial group the diagnosis may be promptly established.

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8. Cushing, Harvey: Surgery of the Head, Philadelphia, W. B. Saunders Company, 1908.

9. Henschen: Verhandl. d. Deutsch. Gesellsch. f. Chir. **41**:271, 1912.

STUDIES ON THE ACIDITY (HYDROGEN ION CONCENTRATION) OF INFANTS' STOOLS *

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The number of investigations of the exact acidity, that is, the hydrogen ion concentration, of infants' stools reported in the literature are comparatively few. When the possible importance of the relation of the acidity of the stools to the general condition of the infant, the rate of growth, the presence of fermentative diarrhea, parenteral infections and many other conditions are considered, it is rather surprising that so few determinations have been reported. The only results which we have been able to find have been recorded in the German literature.

The earliest reported figures on the p_H of infants' stools are those recorded by Eitel[1] in 1917. He found that stools from breast fed infants usually had an acidity of p_H from 4.6 to 5.6, although many values were obtained outside these limits. Stools from infants fed on cows' milk dilutions in the majority of cases gave values which varied from p_H 7.8 to 8.2. He found that buttermilk feeding also gave alkaline values, the average being p_H 8.0. Malt soup, on the other hand, gave acid values usually between p_H 5.4 and 6.0. Freudenberg and Heller,[2] in 1921, found that the p_H of stools from normal breast fed infants generally varied from 4.8 to 5.6. Similar values were obtained by Hess and Scheer[3] in a study on the acidity of infants' stools in relation to dysentery. These authors found that stools from infants fed on buttermilk usually had an acidity from p_H 7.6 to 8.2 and stools from infants on half milk and half water an acidity from p_H 7.2 to 8.6. Whether any carbohydrate was added to the last two types of feeding was not stated. All these authors used the electrometric method for the determination of the p_H of the stools.

Meaning of the Term p_H.—A great deal of work has been done by investigators who have taken a measured portion of an infant's stool and titrated this with an alkali to the point of neutrality. This however determines not only the amount of free acid present, but also

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* Received for publication, Jan. 21, 1924.

* From the wards and nutritional research laboratories of the Hospital for Sick Children and the department of pediatrics of the University of Toronto.

1. Eitel, H.: Ztschr. f. Kinderh. **16**:13, 1917.
2. Freudenberg, E., and Heller, O.: Jahrb. f. Kinderh. **95**:314, 1921.
3. Hess, R., and Scheer, K.: Arch. f. Kinderh. **69**:370 (May) 1921.

a portion of the acid which has already combined with certain bases. At first glance it would appear that if the acid were combined with a base it would be neutral and thus not enter into this titration, but it must be remembered that all salts are not neutral in reaction. One example of this is acid sodium phosphate. It is thus obvious that these titrations have not the same significance or value as the determination of the exact degree of acidity present in the stool.

The question arises as to what constitutes the degree of acidity of a solution. The degree of acidity of a solution depends on one thing; that is, the number of free hydrogen ions present. When a substance such as ordinary salt is placed in a solution it is present in two forms, first, as molecular or undissociated sodium chlorid, which is chemically inert, and secondly, as dissociated (ionized) or chemically active sodium and chlorin ions. Similarly, acids in solution are present in two forms, the molecular or inactive and the dissociated or active forms. All acids, however, on dissociation must give free hydrogen ions (H^+) regardless of the type of acid. Some acids are stronger than others, which simply means that they are more completely dissociated or ionized than the others. Hydrochloric acid is an example of a strong acid, as it is practically entirely dissociated into its hydrogen and chlorin ions. Acetic acid is a weak acid because it is only slightly dissociated (about 2 per cent.); by far the greater part being in the molecular or inactive form.

If the degree of acidity of a solution depends on the number of free hydrogen ions, then the acidity may be measured by determination of the amount of hydrogen ions present in the solution. This is exactly what is done when the acidity is measured. The concentration of the hydrogen ions, and consequently the degree of acidity, is expressed in terms of a fraction of a gram of hydrogen ions per liter of solution. Thus a solution may have an acidity of one tenth of a gram of hydrogen ions per liter or one ten millionth of a gram, or any other amount. It is obvious, however, that this is a very cumbersome method of expressing the acidity of a solution, so the logarithmic notation, first suggested by Sörensen, is used. Thus, a solution containing one tenth of a gram of hydrogen ions per liter is expressed as 10^{-1}, or $1/10^1$; one one-hundredth of a gram as 10^{-2}, or $1/10^2$; one one-thousandth of a gram as 10^{-3}, or $1/10^3$; and so on. Even this, however, is a little cumbersome, so the figures 1, 2, 3, etc., are used in place of 10^{-1}, 10^{-2}, 10^{-3}, etc., preceded by the symbol p_H. Consequently p_H 1, 2 or 3, as the case may be, simply mean a definite amount by weight of hydrogen ions per liter of solution.

A solution with a p_H 1 (or one tenth of a gram of hydrogen ions per liter) is strongly acid; a solution with an acidity of p_H 7 (or one ten-millionth of a gram of hydrogen ions per liter) is neutral and if the concentration is less than one ten-millionth as expressed by p_H 8, 9, 10, etc., it is alkaline. It is beyond the scope of this paper to enter into a discussion of the means by which the amount of hydrogen ions are directly determined, other than to state that this is accomplished by expensive electrometric apparatus.

METHODS FOR THE DETERMINATION OF THE p_H OF SOLUTIONS

As has been stated, the only means of directly measuring the p_H of a solution is by electrometric apparatus. It has been found, however, by careful electrometric measurements that with definite concentrations certain solutions such as monobasic and dibasic phosphates, or sodium citrate and hydrochloric acid, mixed in definite proportions, result in solutions which have a definite and constant p_H. Consequently, it is not difficult to make up solutions with a known hydrogen ion concentration. Having made up these solutions it is easy to develop in each of them a definite color which is constant for each p_H. This is done by the addition of substances called indicators. Each indicator develops its variation in color over a limited range of hydrogen ion concentration. For example, if a few drops of phenolsulphonephthalein are added to solutions whose p_H vary from 6.6 to 8.4 the color ranges from a light yellow to a deep red. If the solution is more acid than p_H 6.6, or more alkaline than p_H 8.4, other indicators must be used. When a set of standards has been made and suitable indicators added, the acidity of an unknown solution may be determined by the addition of an equal amount of the indicator used with the standard, and subsequent comparison of the color developed with that present in the standard solution. This constitutes what is known as the colorimetric method. It has the advantage over the electrometric method in that it does not require an expensive apparatus and is not so time consuming. At the same time it gives results which are comparatively accurate.

The value of the colorimetric method for the determination of the p_H of stools is seriously impaired because of the difficulty in obtaining a clear and colorless fecal extract. It is obvious that the presence of turbidity, or color, interferes with the accuracy of the method. Also the presence of proteins interferes with the action of some indicators. Howe and Hawk[4] found it practically impossible by filtration through paper or by centrifugation to obtain an extract which was not turbid or colored. Nelson and Williams[5] attempted to overcome this difficulty by centrifuging and filtering the stool extract through two thicknesses of filter paper. Rettger and Cheplin[6] also used the same procedure. The values obtained, however, by this method on normal adult stools were much more acid than those recorded by Howe and Hawk, and later by Robinson,[7] all of whom used the electrometric method. Most investigators, on account of the above mentioned difficulties, have used the electrometric method for the determination of the p_H of stools.

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[4] Howe, P. E., and Hawk, P. B.: J. Biol. Chem. **11**:129, 1912.

[5] Nelson, C. F., and Williams, J. L.: J. Biol. Chem. **28**:231 (Dec.) 1916.

For the present investigation of the p_H of infants' stools, we have utilized a simple and well known procedure by means of which colorimetric determinations have been made with rapidity and accuracy. In 1915, Levy, Rowntree and Marriott[8] suggested the use of collodion sacs for the determination of the p_H of blood. The blood was dropped into these sacs and dialyzed for five minutes. The dialysate was found to be free from proteins and coloring matter but contained blood salts, and was well adapted for use with indicators. In 1920, Kramer and Greene[9] utilized collodion sacs for the colorimetric determination of the p_H of milk and obtained results that were found to be quite accurate when checked by electrometric determinations. It is obvious that the same principle can be used for the determination of the acidity of stools, and in the following paragraphs are given the details of the procedure devised by one of us (F.F.T.) for the present investigation.

PROCEDURE FOR DETERMINATION OF p_H OF STOOLS

Standard solutions from p_H 5 to p_H 8.3 are obtained by the use of anhydrous dibasic sodium phosphate and acid potassium phosphate. Tenth normal solutions of each are used. The amounts used (Table 1) were obtained from a curve prepared by Sörensen.[10] Tenth molar sodium citrate and tenth normal hydrochloric acid are used to obtain solutions from p_H 3 to p_H 4.8. The tenth molar sodium citrate is made by dissolving 21.008 gm. citric acid in 200 c.c. of normal sodium hydroxid and adding water to 1,000 c.c. The amounts used (Table 2) were also obtained from a curve prepared by Sörensen. The indicators used are as follows: Methyl orange from p_H 3 to 4.4; methyl red from p_H 4.6 to 5.6; dibromorthocresolsulphonephthalein from p_H 5.8 to 6.4; phenolsulphonephthalein from p_H 6.6 to 7.6 and orthocresolsulphonophthalein from p_H 7.8 to 8.3. The standards may be used for over a month without the colors changing, with the exception of the methyl red, which generally fades slightly within a week's time. Alphanaphthylaminazosulfanilic acid was tried in place of methyl red but it was also found to fade, with the added disadvantage that the color changes were not so marked.

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[6] Rettger, L. F., and Cheplin, H. A.: A Treatise on the Transformation of the Intestinal Flora with Special Reference to the Implantation of *Bacillus Acidophilus,* New Haven, Yale University Press, 1921.

[7] Robinson, C. S.: J. Biol. Chem. **52**:445 (June) 1922.

[8] Levy, R. L.; Rowntree, L. G., and Marriott, W. McK.: A Simple Method for Determining the Hydrogen-Ion Concentration of the Blood, Arch. Int. Med. **16**:389 (Sept.) 1915.

[9] Kramer, B., and Greene, C. H.: Proc. Soc. Biol. Chem. (Dec.) 1920, reported in J. Biol. Chem. **46**: XXXVIII, 1921.

[10] Neuberg, C.: Der Harn, Berlin, Julius Springer, **2**:1574, 1911.

TABLE 1.—*Amounts of Tenth Normal Dibasic Sodium Phosphate and Tenth Normal Monobasic Potassium Phosphate Necessary to Obtain Standard Solutions from P_H 5.0 to P_H 8.3.*

p_H	C.c. Tenth Normal $Na_2HPO_4 + 2H_2O$	C.c. Tenth Normal KH_2PO_4	p_H	C.c. Tenth Normal $Na_2HPO_4 + 2H_2O$	C.c. Tenth Normal KH_2PO_4
5.0	0.04	3.96	6.8	2.00	2.00
5.2	0.08	3.92	7.0	2.48	1.52
5.4	0.14	3.86	7.2	2.92	1.08
5.6	0.20	3.80	7.4	3.28	0.72
5.8	0.32	3.68	7.6	3.54	0.46
6.0	0.48	3.52	7.8	3.76	0.24
6.2	0.74	3.26	8.0	3.90	0.10
6.4	1.08	2.92	8.3	4.00	0.00
6.6	1.48	2.52			

TABLE 2.—*Amounts of Tenth Molar Sodium Citrate and Tenth Normal Hydrochloric Acid Necessary to Obtain Standard Solutions from P_H 3.0 to P_H 4.8*

p_H	C.c. Tenth Normal Sodium Citrate	C.c. Tenth Normal HCl	p_H	C.c. Tenth Normal Sodium Citrate	C.c. Tenth Normal HCl
3.0	1.60	2.40	4.0	2.24	1.76
3.2	1.70	2.30	4.2	2.44	1.56
3.4	1.80	2.20	4.4	2.72	1.28
3.6	1.94	2.06	4.6	3.04	0.96
3.8	2.08	1.92	4.8	3.48	0.52

Collodion sacs are prepared practically according to the directions outlined by Levy, Rowntree and Marriott.[8] Half an ounce (14 gm.) of collodion is dissolved in 250 c.c. of a mixture of equal quantities of ether and ethyl alcohol. It dissolves, with occasional shakings, in forty-eight hours. A small test tube (1.3 cm. inside measurement, by 12 cm.) is filled with this mixture, inverted and the contents allowed to run out slowly. Care must be taken to rotate the tube in order to secure a uniform thickness throughout. The tube is clamped in the inverted position and allowed to stand from ten to fifteen minutes. It is then filled a few times with cold water. A knife blade is run around the upper rim so as to loosen the sac from the rim of the test tube, and then a fine glass rod is gently inserted between the sac and the wall of the test tube. The tube should be kept full of water and by gentle manipulation with the glass rod, the sac can be separated from the tube.

It should then be preserved by complete immersion in water. The sacs can be used again and again until they are torn or otherwise destroyed.

The stools were obtained from the infant by inserting a glass rod in the rectum and when being passed were collected directly in a small evaporating dish. They were then put in the ice box. It was found that their p_H did not change during the next twenty-four hours. However, the determinations were generally made the day the specimens were obtained. A small amount of freshly distilled and boiled water (from 15 to 20 c c.) is added to the fecal material in each evaporating dish and thoroughly mixed by means of a glass rod. The minimum amount of stool necessary is a piece about the size of a large pea. This emulsion is poured into the collodion sac which in turn is inserted in a test tube (1.7 cm. inside measurement by 15 cm.) containing 10 c.c. of the boiled distilled water. Dialysis is allowed to proceed for from twenty to thirty minutes, the sac being then removed leaving 10 c.c. of a clear and colorless fluid which has the same p_H as that of the stool. Four cubic centimeters of the dialysate are poured into a test tube of the same size as that of the tubes containing the standard solutions, and a few drops of the indicator is added. If the proper indicator is not selected at the first trial there is sufficient dialysate left for repetition. The color developed is compared with that in the standard tubes.

The method as outlined above has the advantage of requiring comparatively little time. It also gives results which for clinical purposes compare favorably with those obtained by the electrometric method (Table 3).

Table 3.—*Comparison of the Results Obtained by the Colorimetric Method and the Electrometric Method for the Determination of the p_H of Stools* *

Standard Solutions	Colorimetric Method	Electrometric Method	Stools No.	Colorimetric Method	Electrometric Method
p_H 3.0	—	3.06	1	5.8	5.76
p_H 4.6	—	4.64	2	6.2	6.16
p_H 5.6	—	5.66	3	6.8	6.78
p_H 6.8	—	6.82	4	7.6	7.50
			5	8.0	8.00

* The authors are indebted to P. J. Moloney, of the Connaught Laboratories, for the electrometric determinations.

RESULTS

During last summer, over 1,300 determinations were made of the p_H of infants' stools. The object of the investigation was not to study the effect on the p_H of the stools of carefully prepared variations in the diet, but rather to determine the acidity as a routine procedure over a considerable period of time. Although it was quite evident at the beginning of this work that a number of the results would be of little use, still it was hoped that valuable information might be obtained where possibly least expected. In our opinion the results obtained have justified the procedure.

With the exception of a few stools from newly born breast fed infants, all the specimens were obtained from artificially fed babies. They varied in consistency and appearance from that of loose green diarrheal stools to that of hard brown constipated stools. It was soon found that the presence of mucus produced an alkaline reaction. As a result of this, many diarrheal stools which contained mucus gave an alkaline reaction when it was quite evident that the underlying condition was an increased acidity of the intestinal contents (Chart 1). This is probably the explanation of some of the conflicting statements made by older writers that diarrheal stools, under fermentative conditions, may have an alkaline reaction. It was also found that the brown, formed, constipated stool was not nearly so alkaline as the pasty stool,

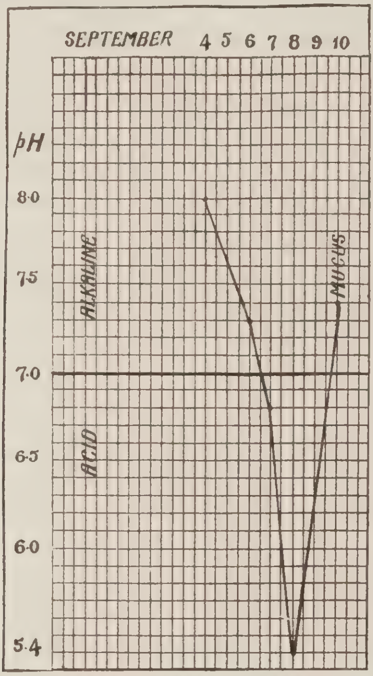

Chart 1 (Case J. F.).—An alkaline reaction produced by the presence of mucus. September 6, the stool was brown, pasty; September 7, yellow, pasty; September 8, yellow, curdy; and September 10, yellow, fluid with mucus.

and in other cases it was observed that reactions as alkaline as p_H 8.3 were obtained with stools of a fluid to semifluid consistency. This simply demonstrates that the firmness of a stool may give little indication of the degree of acidity present. Most of the stools with a reaction more acid than p_H 6.6, with the exception of diarrheal watery stools, were of a curdy consistency and had an acid odor. Values were obtained from the stools of artificially fed babies, which varied from p_H 4.6 to slightly more alkaline than p_H 8.3. As stools were rarely encountered with an alkalinity of more than p_H 8.3 the standards were not extended beyond this value.

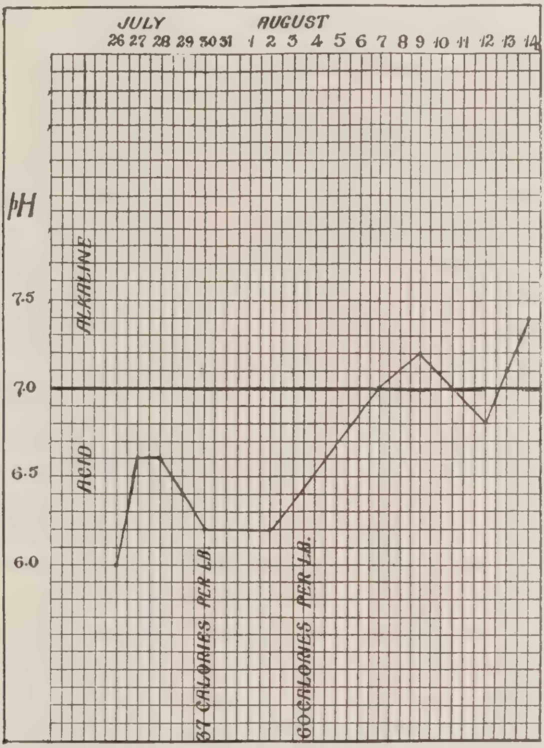

Chart 2 (Case G. L.).—Aged 2 months, weight 8 pounds (3,638 gm.). The reaction of the stools from acid to alkaline may be changed by the addition of carbohydrate to protein milk. The diet on July 27 was 30 ounces (850 gm.) protein milk (powdered preparation) two-thirds strength; July 30, ⅔ ounce (19 gm.) of casic was added, and on August 4, 1 ounce (28 gm.) of corn syrup was added.

Determinations to the extent of twelve in number were made of the acidity of stools from breast fed infants. As practically no infants were admitted to the hospital during last summer who received breast milk exclusively, specimens were obtained from the Burnside Clinic of the new-born. All the infants were under 2 weeks of age. The p_H was found to be singularly constant. It varied only from p_H 4.7 to 5.1 in the twelve specimens examined.

In a general way, it was found that the degree of acidity of the stools was largely dependent on the type of food used. The stools from the normal breast fed infants mentioned above had an acidity of about p_H 5.0. Infants fed on buttersoup [11] generally had stools with a p_H of about from 5.8 to 6.2, while the stools from infants fed on protein milk, cows' milk dilutions with added carbohydrate, or whole soured milk with added carbohydrates were generally more alkaline than p_H 7.0. It has usually been considered that protein milk with its low sugar content would produce an alkaline stool, while a feeding with

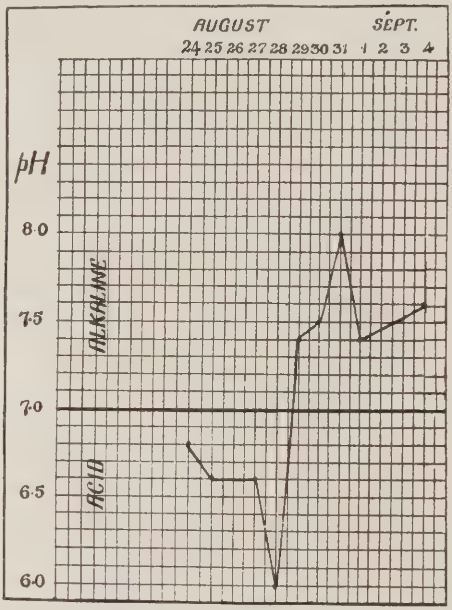

Chart 3 (Case R. N.).—Aged 12 months. Weight 17 pounds (7,711 gm.). The reaction of the stools from acid to alkaline may be changed by the addition of carbohydrate to soured milk. Until the afternoon of August 27, this infant was on 40 ounces (1,134 gm.) of 2 per cent. soured milk and 1 ounce (28 gm.) of dextri maltose. The stools, which were yellowish green in color, contained a lot of fat curds. They could not be characterized as good stools. On the afternoon of August 27, the feeding was changed to 25 ounces (718 gm.) of 4 per cent. soured milk, and 3½ ounces (100 gm.) of granulated sugar. By August 30, the stools were of a yellow-gray pasty appearance. It is to be noted that the total amount of fat given was practically unchanged.

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[11] Brown, A.; Courtney, A. M., and MacLachlan, I. F.: A Clinical and Chemical Study of Butter Soup Feeding in Infants, Am. J. Dis. Child. **24**:368 (Nov.) 1922.

a high carbohydrate content would produce an acid stool. In this connection some very surprising results were obtained. In certain instances it was found that infants fed on protein milk or soured milk had acid stools which remained acid until carbohydrates were added to the diet (Charts 2 and 3). Also it was found that the most alkaline stools were obtained from infants fed on whole soured milk with a total carbohydrate content as high as 20 per cent. No consistent difference was found in the acidity whether the carbohydrate was added in the form of corn syrup, dextri maltose or cane sugar. The values obtained with one baby (W.B.) serve as an example. This infant was studied over a period of three and a half months. The diet consisted of whole soured milk with added carbohydrate up to a total content of 12 per cent. for the first two and a half months, then to just under 20 per cent. for the following month. During this period the acidity of the

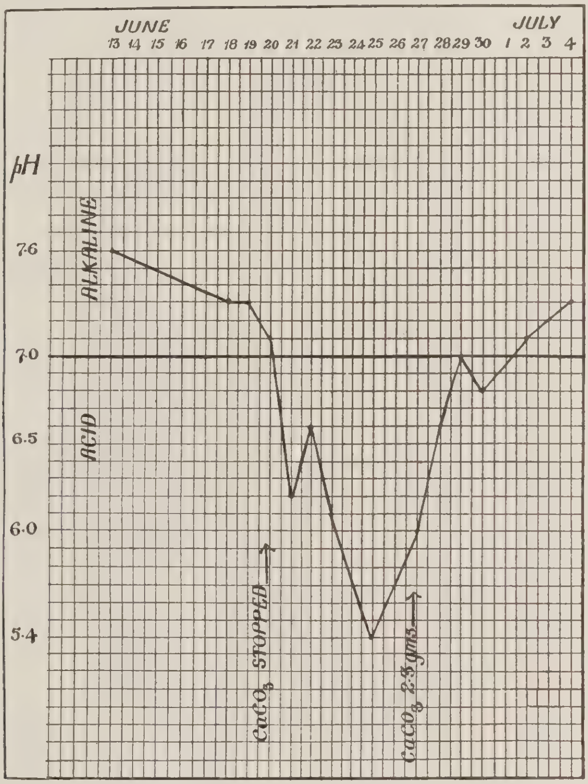

Chart 4 (Case J. D.).—The effect produced on the acidity of the stools by the addition of calcium carbonate to a diet containing a small amount of calcium salts. This infant was fed 14 ounces (396 gm.), of buttersoup, 7 ounces (198 gm.) of whole milk and 2.3 gm. calcium carbonate. The calcium carbonate was omitted and then replaced with the above result.

stools was determined sixty-three times. Of these sixty-three determinations, only four were more acid than p_H 7.6. The values generally ranged from p_H 7.6 to 8.3. The stools were large, brownish, gray and soapy and when the inner part was exposed had a greasy appearance.

The effect of the addition of calcium carbonate to the food was determined in a few instances. It was found in certain cases that the addition of fairly large quantities (2.3 gm. per day) of the salt to buttersoup feeding made the stool more alkaline (Chart 4). On the other hand, in diarrheal conditions it produced practically no change. Although not sufficient cases were studied to draw authoritative conclusions, still, it appears that while the addition of calcium carbonate to the food in normal cases makes the stool more alkaline, in diarrheal conditions it has little effect.

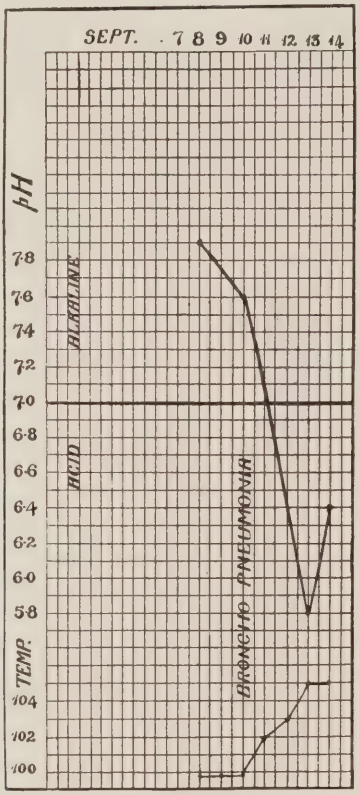

Chart 5 (Case R. S.).—The change produced in the acidity of the stool by the presence of a parenteral infection.

Observations were made on the effect of parenteral infections in a large number of cases. In the majority of instances the acidity of the stools increased and the smooth and pasty consistency changed to a slightly loose and curdy consistency (Chart 5). In other infants the presence of parenteral infections seemed to have no effect either on the p_H of the stools or on their consistency (Chart 6). In one infant rather unusual results were obtained. This baby (Chart 7) developed pyelitis and the stool, observed daily, showed the following changes: August 30, brown semi-formed; August 31, loose, grayish curdy; September 1, brown fluid with mucus; September 2, very watery with a few green curds and mucus. Yet in this case the p_H never became more acid than 7.1. It is probable that the early production of mucus more than neutralized the effects of any acids present. It is of interest to note that shortly after this, the infant showed evidences of a prolapse of the rectum, which condition may have been a factor in the early production of mucus. From the foregoing observations it appears that parenteral infections generally cause an increased acidity of the stool, although there are many exceptions to this rule.

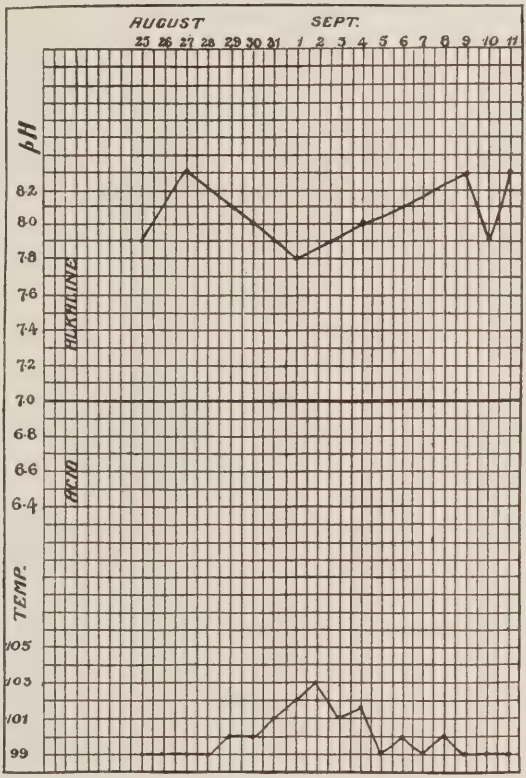

Chart 6 (Case W. B.).—The acidity of the stool is practically unaltered in some cases in the presence of a parenteral infection. The consistency of the stools in this case did not change during the infection.

The question arises whether the acidity of the stool has any connection with the rate of growth of the infant. The answer may be both in the negative and the affirmative. It is well known that infants gain well on foods which normally produce acid stools, such as breast milk, buttersoup and malt soup. It is also obvious that they may gain just as well on foods which normally produce alkaline stools, such as whole milk dilutions or whole soured milk, with added carbohydrates. It was found however, that if the acidity was greater than that which is normally found with the particular type of food given, the infant did not do well.

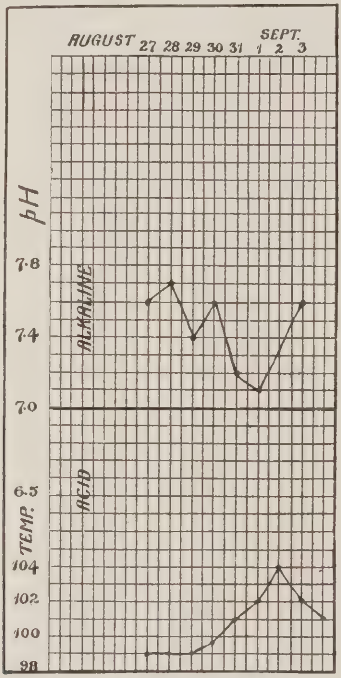

Chart 7 (Case K. S.).—This infant, in the presence of a parenteral infection, developed loose watery stools with a few green curds and mucus. The stools did not show the preliminary acid reaction before the presence of mucus was noted.

Some further observations made during the course of these investigations are of interest. When the food was changed from buttersoup to either whole milk dilutions or whole soured milk, with added carbohydrates, the p_H of the stool changed with surprising rapidity. If the change in the food was made at 2 p. m., the stools obtained the next day at 9 a. m. were of a different consistency and of a much more alkaline reaction (Chart 8). Another point of interest observed was that in occasional cases when an infant was given a food which would normally produce an alkaline stool, the reaction would be acid for some days, then for no apparent reason the stool would suddenly change in consistency and become alkaline (Chart 9). A third observation of interest was that in certain infants the acidity of the stools showed wide daily variations. No apparent cause for this was found (Chart 10).

CONCLUSIONS

It is now widely recognized that of the three main organic constituents of infant's food, that is, the fats, the carbohydrates and the proteins, it is chiefly the carbohydrates that are concerned with the production of acid. This production of acid is the result of the fermentative action of microorganisms which break down the carbohydrates into lactic, acetic, formic, butyric and succinic acids. Lactic acid is the acid that is produced in the largest quantities, although occasionally a considerable amount of acetic acid may be present. Only traces of the other acids are found.[12]

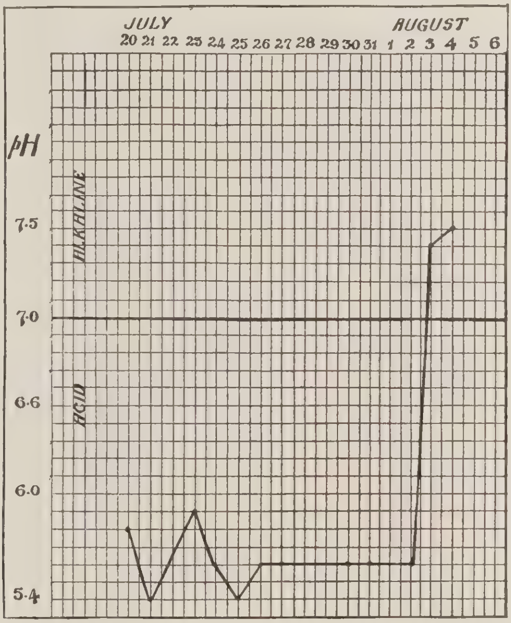

Chart 8 (Case B. J.).—The rapid change in the acidity of the stools with a change in the food. On August 2, the food was changed from buttersoup to a whole cows' milk dilution with added carbohydrate.

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12. Tobler, L., and Bessau, G.: Allgemeine Pathologische Physiologie der Ernahrung und des Stoffwechsels im Kindersalter, Wiesbaden, J. F. Bergmann, 1914, p. 183.

Fats are normally broken down by some of the intestinal secretions into the higher fatty acids and glycerine. These higher fatty acids, however, are nonirritating, or at most only slightly so. It has not been conclusively demonstrated that bacteria can split fat or break down the nonirritating higher fatty acids into the irritating lower fatty acids.[13] At the same time the presence of fat and the higher fatty acids may have a stimulating effect on the growth of bacteria and thus indirectly increase the acidity.[13]

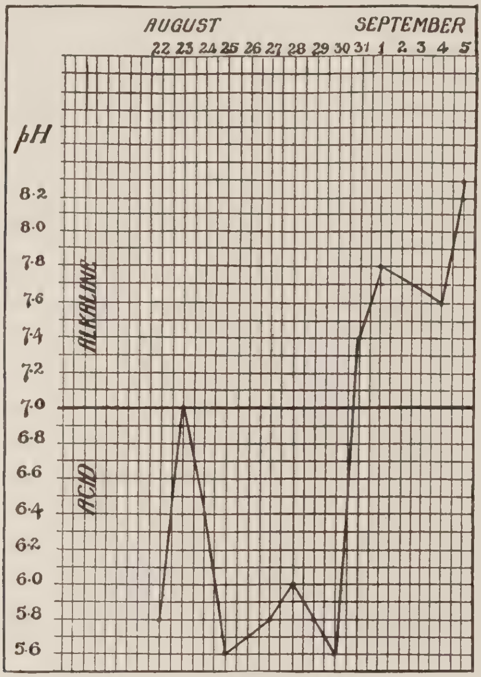

Chart 9 (Case M. K.).—On August 22, the food in this case was changed from 20 ounces (567 gm.) of 2 per cent. soured milk, and ½ ounce (14 gm.) of corn syrup to 20 ounces (567 gm.) of 4 per cent. soured milk, and 3 ounces (85 gm.) of dextri maltose. A marked change in the acidity of the stool did not occur until August 30, eight days later. No reason was found for this delayed action.

The proteins are affected by many microorganisms and various products are found such as indol, skatol, certain amin bases, and ammonia. From our standpoint we are chiefly interested in the ammonia production on account of its alkaline reaction. Certain acids may be formed in small quantities but their effect is greatly overbalanced by that of the ammonia produced. It is thus evident that bacterial action on proteins, with the resultant liberation of ammonia, tends to produce an alkaline reaction.

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[13] Schiff, E., and Kochmann, R.: Jahrb. f. Kinderh. **99**:181 (Sept.) 1922.

From the foregoing statements it would appear that the reaction of a stool depends largely on the ratio of the carbohydrates to the protein in the food. Although this is true, nevertheless there are a number of other factors which greatly influence the reaction of the feces. These will be discussed briefly.

It is known that, normally, bacterial growth in the intestinal canal is almost entirely limited to the lower part of the ileum and the large intestine. As the production of acid from carbohydrates is accomplished by the action of microorganisms it is obvious that this production of acid must occur in the lower ileum and the large intestine, the so-called zone of fermentation. If normally no fermentation occurs in the upper part of the small intestine, and sugars can be absorbed by this part of the intestine, it is clear that one of the important factors in the production of acid is not the amount of sugar in the food but the amount of sugar which reaches and remains in the zone of fermentation. This point has been strongly emphasized by Bessau.[14] Freudenberg and Heller [15] have demonstrated most clearly that the rate

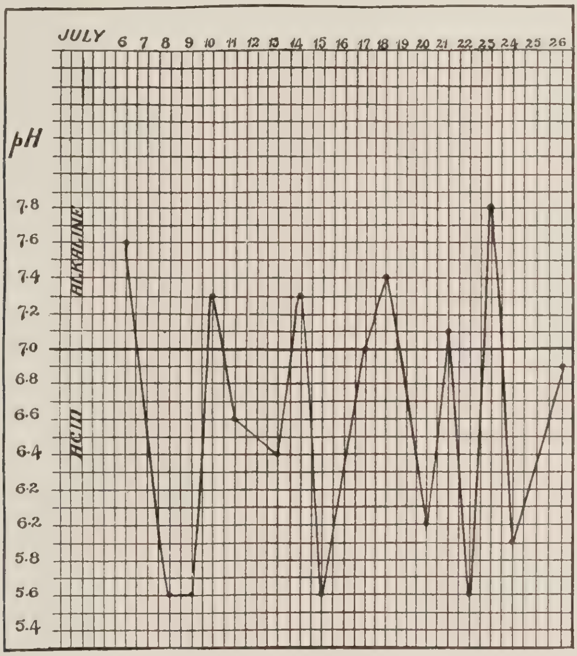

Chart 10 (Case H. S.).—The wide daily variations in the acidity of the stool which was encountered only occasionally. No apparent cause was found for these variations.

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14. Bessau, G.: Jarhb. f. Kinderh. **92**:14, 1920.
15. Freudenberg, E., and Heller, O.: Jahrb. f. Kinderh. **96**:49, 1921.

of absorption of a sugar has a definite effect on the acidity of the stool. Utilizing the fact that caramel is poorly absorbed by the intestinal mucosa,[16] Freudenberg and Heller fed an infant a whole cows' milk dilution containing 80 gm. of caramelized cane sugar. The caramelization was accomplished by heating the cane sugar in an open pan until it was of a dark brown color. The p_H of the stool was found to vary from 4.7 to 5.0. The cane sugar was then added without being caramelized and the stool promptly became alkaline with a p_H of 6.7 to 7.4. It is obvious, therefore, that the rate of absorption of the carbohydrate by the intestine is an important factor in the production of acid.

As the production of acid from carbohydrates is the result of bacterial action, different bacteria may produce different degrees of acidity. That this is so has been clearly demonstrated. Michaelis and Marcora,[17] Clark,[18] Scheer [19] and others have found that the colon bacillus will not produce an acidity greater than p_H 5.0 and that when the acidity is greater than this (p_H 4.6) the colon bacillus is killed. *Streptococcus lacticus* produces an acidity of p_H 4.2 to 4.6 while the *Bacillus bifidus* produces an acidity as great as p_H 3.7.[20] It is well known that in alkaline stools the bacterial flora is largely gram negative while in acid stools the flora is preponderantly gram positive (*B. bifidus, B. lacticus, B. acidophilus,* etc.). The question at once arises, is the acidity of the stools the result of an infection and subsequent growth of an acid producing organism, or is the presence of these organisms secondary to other factors? It would appear most reasonable to assume that acid stools are the result of an infection, and the resultant preponderant growth of the acid producing gram positive organisms. This question has been investigated at some length by many bacteriologic workers. Their results will not be discussed here. However, a series of experiments from the chemical standpoint have been reported by Scheer [20] which are most interesting. He inoculated various milk media with stools from infants fed on breast milk and also from infants fed on protein milk. In three days the acidity of the media had reached p_H 3.7 regardless of the type of stool with which it had been inoculated. It is evident that acid producing organisms were present in both types of stools but that in the protein milk stool the conditions were not favorable for their proliferation, with the resultant production of acid. It seems

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16. Grafe: München. Med. Wchnschr., 1914; quoted by Freudenberg, E., and Heller, O.: Jahrb. f. Kinderh. **96**:49, 1921.
17. Michaelis, L., and Marcora, F.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **14**:170, 1912.
18. Clark, W. M.: J. Biol. Chem. **22**:87, 1915.
19. Scheer, K.: Biochem. Ztschr. **130**:545, 1922.
20. Scheer, K.: Ztschr. f. Kinderh. **29**:253 (July) 1921.

probable then that the acidity of the stool is not the result of an infection by any particular type of organism, but rather the result of conditions which allow one or another definite type of organism to grow.

The reaction of the stool can be altered by the addition of certain inorganic substances to the diet. This has been demonstrated by Scheer and Muller,[21] who added alkaline sodium phosphate to breast milk and changed the reaction of the stool from p_H 5.0 to p_H 7.1. In the present paper, it is shown that the addition of a large amount of calcium carbonate may change the reaction of the stool (Chart 4). The explanation of the change is that the acids present react with these bases, and produce salts which have only a slight degree of acidity (buffer influence).

As already mentioned, the presence of proteins tends to produce an alkaline reaction on account of the production of ammonia by bacterial action. From the discussion so far, it would appear that the reaction of the stool depends on the ratio of the amount of carbohydrate present in the zone of fermentation on one hand, to the amount of protein and bases on the other hand. It has been shown that the type of carbohydrate may influence the acidity of the stool by being poorly absorbed in the upper part of the small intestine and thus reaching the zone of fermentation in fairly large quantities. Also, if the condition of the cells in the intestinal wall is such that they absorb the carbohydrate poorly, regardless of the type of carbohydrate in the food, then the amount of sugar available for fermentation would be increased, with a resultant increase in the acidity of the stool. In our opinion this is probably one of the most important factors in the production of acid in the intestinal canal.

There are at least two other factors which may be of considerable importance in determining the acidity of the stools. The first is the amount of intestinal secretion, which may have a marked effect on account of its alkaline reaction. The second is that in many pathologic conditions it is probable that the zone of fermentation extends farther up the intestinal canal than is normally the case.

It has been shown by Scheer [20] that there is enough carbohydrate present in protein milk to allow the production of an acidity of p_H 3.7 when inoculated with infants' stools. Consequently, if protein milk is fed to an infant, enough carbohydrate is being given to produce an acidity of p_H 3.7 if it is not absorbed before it reaches the zone of fermentation. It has been stated by Finkelstein [22] that at least 3 per cent. carbohydrate, and frequently more than this amount, should be present in the food in order to enable the metabolism of the body to proceed in the normal manner. Then, if in an effort to correct an intestinal acidity an infant is fed protein milk with its low sugar and high protein and base content for a sufficient period to allow the low sugar to interfere with the nutrition of the intestinal cells, it is possible for the sugar to reach the zone of fermentation with the resultant production of acid. The addition of sugar to the diet might then stimulate the intestinal cells, so that there would be an increased absorption of the sugar and a resultant decrease in the acidity of the stool. Also, stimulation of the intestinal cells from the increased sugar content in the food might influence the amount of alkaline intestinal secretions and also the length of the zone of fermentation.

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[21] Scheer, K., and Muller, F.: Jahrb. f. Kinderh. **101**:143 (March) 1923.

[22] Finkelstein, H.: Lehrbuch der Sauglings krankheiten, Berlin, Julius Springer, 1921, p. 291.

It is of interest to note the results obtained in the present investigation in the light of the above remarks. In Chart 2 we see that an infant fed on protein milk had stools with an acid reaction. The addition of sugar to the diet changed the reaction of the stool to the alkaline side of neutrality. A similar result is shown in Chart 3. This infant was on a diet containing 6.5 per cent. carbohydrate and the reaction of the stools was quite acid. The carbohydrate was increased to 18 per cent. and the stools promptly became more formed and had an alkaline reaction. Numerous other infants were fed whole soured milk with added carbohydrate up to a total content of 20 per cent., and in the majority of cases the stools were of a smooth and pasty consistency with a strongly alkaline reaction. A possible explanation for this surprising result is that the high carbohydrate so stimulated the intestinal cells that the absorption of sugar occurred very rapidly and thus lessened the opportunity for fermentation. The possibility must also be considered that the stimulated intestinal cells diminished the extent of the zone of fermentation and also produced a larger quantity of alkaline secretions. A further explanation might be found in the work of Wolff [23] who showed that when the concentration of sugar was greater than 10 per cent., fermentation was hindered.

The production of an acid stool by a parenteral infection may be explained on the ground that the vitality of the intestinal cells is diminished by the infection. This results in a lessened absorption of carbohydrate, and consequently an increase in the amount available for fermentation with the resultant production of acid. No doubt the zone of fermentation is also increased.

From the foregoing it might be assumed that we are advocating the use of high sugar diets in combination with whole soured milk to combat diarrheal conditions. While it is beyond the scope of this paper to enter into any discussion of this aspect of the problem, we simply draw attention to the fact that in certain diarrheal conditions the use of a

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23. Wolff, E.: Ztschr. f. Kinderh. **31**:226, 1921.

concentrated high carbohydrate food will produce constipated alkaline stools. Similar results have been reported by Davidsohn and Rosenstein.[24] In many other cases, the use of this type of feeding will be followed by strongly acid watery stools and disastrous results.

SUMMARY

1. A simple procedure for the determination of the p_H of infants' stools has been described.

2. In the present investigation, over 1,300 determinations of the p_H of infants' stools have been made.

3. The p_H of stools from normal newly born breast fed infants was found to be singularly constant, varying from 4.7 to 5.1.

4. The acidity of stools from artificially fed infants was found to vary from p_H 4.6 to somewhat more alkaline than p_H 8.3.

5. An acidity as great as p_H 4.6 was encountered in artificially fed infants only in severe diarrheal conditions. Infants fed on buttersoup generally had stools with an acidity of about p_H 6.0. Infants fed on protein milk, cows' milk dilutions with added carbohydrates, and whole soured milk with added carbohydrates generally had stools more alkaline than p_H 7.0.

6. Whole soured milk, with added carbohydrates up to a total content of 20 per cent., generally produced strongly alkaline stools.

7. No difference was consistently observed in the acidity of the stool, whether the added carbohydrate was in the form of corn syrup, dextri maltose or cane sugar. In the present investigation, the effect produced by other sugars was not determined.

8. The degree of acidity of the stools was generally increased in the presence of parenteral infections.

9. Based on the present work and the work of others, the factors which influence the acidity of the stools have been discussed. From the chemical standpoint the acidity apparently depends on the ratio, *in the intestinal zone of fermentation,* of the carbohydrate on one hand to the protein and base on the other. The amount of carbohydrate in the zone of fermentation, apparently is influenced by the extent of the zone of fermentation, by the type of carbohydrate and by the state of health of the intestinal cells.

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[24] Davidsohn, H., and Rosenstein, S.: Ztschr. f. Kinderh. **35**:207 (June) 1923.

THROMBOCYTOPENIC PURPURA HEMORRHAGICA SUCCESSFULLY TREATED BY SPLENECTOMY *

REPORT OF A CASE

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Our purpose in this report is to add another case to the small number of cases of thrombocytopenic purpura cured by splenectomy, in order to emphasize the extreme importance of this curative measure.

Kaznelson,[1] believing that essential thrombocytopenic purpura was due to the thrombolytic action of the spleen, had splenectomy performed as a curative measure. The result was very gratifying. The bleeding immediately stopped, and an extremely ill patient became rapidly converted into an apparently healthy person. Not only did the bleeding stop, but several of the pathologic phenomena, relating to blood coagulation characteristic of the disease, at once disappeared. Brill and Rosenthal, in New York, determined to make use of the same method, and obtained the same brilliant results.

We do not intend to discuss either the rationale of this surgical procedure nor to report on the literature and the pathogenesis of thrombocytopenic purpura. The reader interested is referred to recent articles by Brill and Rosenthal, American Journal of the Medical Sciences, October, 1923; Archives of Internal Medicine, December, 1923.

When a child entered the pediatric service with the clinical picture and hematologic findings characteristic of the thrombocytopenic form of purpura hemorrhagica, we decided on a splenectomy as a radical cure. The detailed case report is presented herewith.

REPORT OF CASE

History.—F. F., a girl, aged 8 years, of Italian parentage, was admitted to the Pediatric Service of Mount Sinai Hospital on July 19, 1923. The patient's chief complaints were that for the last three years she had had many epistaxes, and that ecchymoses frequently appeared on the body.

The family history was negative, there were no other members who showed any tendency to hemorrhage. Four brothers and one sister are alive and well. The past history was also negative, the patient never having been sick until the present illness.

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* Received for publication, Jan. 21, 1924.

* From the pediatric service of Mount Sinai Hospital.

[1] Kaznelson: Wien. klin. Wchnschr. **29**:1451, 1916; Ztschr. f. klin. Med. **87**:133, 1919.

Present Illness.—For the last three years the child has had many epistaxes. These last from one day to several weeks. They come on suddenly, spontaneously and usually require nasal packing. On the least trauma, and at times apparently spontaneously, ecchymoses appear on the skin. For the last six weeks there has been a daily nosebleed. She has had several convulsions during the last three years, the latest one seven months ago. The stools are black only after nosebleeds. There was no hematemesis. The patient suffered from transient febrile periods. There was no palpitation or dyspnea.

Physical Examination.—The patient's general condition was good. She was pale, but did not appear acutely ill. The skin showed many black and blue spots of various sizes scattered over the surface of the body. The mucous surfaces were pale; the nasal mucosa failed to show any ulcerations or dilated veins. The lymph nodes were not palpable. The heart was not enlarged. There was a faint systolic murmur heard over the pulmonic area. The lungs were normal. The spleen was just felt at the costal border. The liver, felt 3 cm. below the costal border, was smooth and of normal consistency. The abdomen was soft, no masses were felt. The urine was normal. The blood Wassermann test was negative.

Blood Examination.—Hemoglobin, 60 per cent., red cells 5,200,000; white cells 4,800; polymorphonuclear neutrophils 58 per cent., lymphocytes 42 per cent.; bleeding time, twenty minutes; coagulation time, four minutes; tourniquet test positive. Clot retraction was absent (even after six hours); reticulated cells, 5.2 per cent.; platelets 11,000.

During the time the patient was under our observation there was blood continually oozing from the nares, and many new ecchymotic spots appeared. Splenectomy was decided on and performed, July 31, by Dr. Harold Neuhof. The child stood the operation very well but on the following day developed a right lower pneumonia. For four days she had fever and appeared sick, becoming slightly icteric on the third day. Eventually the temperature disappeared and the signs in the chest cleared up. She made an uneventful recovery, and was discharged from the hospital September 14.

Pathologic Report.—Macroscopically, the specimen consisted of a spleen, weighing 180 gm. and measuring 9.4 by 4.4 cm. It appeared to be about normal in size or perhaps slightly increased for the age of this patient (8 years). The hilum did not contain any hemolymph nodes. The surface was smooth and glistening, the cut surface appeared normal. Malpighian bodies appeared normal.

Pathologic Diagnosis.—Slight hypertrophy of Malpighian bodies. Infiltration of pulp with polymorphonuclear neutrophils and eosinophils.

The table shows a list of the blood examinations taken during and following the patient's stay in the hospital.

The foregoing history shows that we were dealing with a typical case of chronic hemorrhagic purpura with marked reduction in the number of the platelets. Not only the history of chronic bleeding but also the laboratory findings were characteristic, there was markedly prolonged bleeding time; coagulation was normal; clot retraction was absent; the platelets were greatly diminished; the white cells were morphologically normal and present in normal numbers. Experience having shown that cases of this nature were cured by splenectomy, we decided on operation, especially as the patient had been under medical treatment for three years without any beneficial results. The splenec-

Blood Examinations During and Following Patient's Stay in Hospital

	July 20	July 26	July 31 Before Operation	July 31 One Hour Post-operative	Aug. 1	Aug. 4	Aug. 6	Aug. 7	Aug. 8	Aug. 9	Aug. 20	Sept. 1	Oct. 20	Dec. 10
Hemoglobin (Sahli)	60%	60%	60%	60%	66%	56%	57%	56%	58%	61%	75%	80%	80%	85%
Red blood cells	5,200,000	5,400,000	4,500,000	4,500,000	5,600,000	4,800,000	4,800,000	4,300,000	4,300,000	4,400,000	....	....	....	....
White blood cells	4,800	8,300	....	21,600	42,600	16,800	17,400	28,600	17,800	18,600	9,600	....	....	....
Polymorphonuclears	58%	....	....	87%	91%	89%	78%	89%	85%	75%	60%	....	....	....
Lymphocytes	42%	....	....	10%	6%	8%	6%	5%	8%	17%	23%	....	....	....
Eosinophils	....	....	....	....	....	....	10%	3%	4%	7%	9%	....	....	....
Mononuclears	....	....	....	3%	3%	3%	6%	3%	3%	1%	8%	....	....	....
Platelets	11,000	2,000	....	42,000	80,000	220,000	120,000	90,000	90,000	100,000	100,000	90,000	90,000	60,000
Reticulated reds	5.2%	....	....	....	....	....	....	....	....	....	....	....	....	....
Bleeding time	20 min.	15 min.	16 min.	5 min.	1 min.	1½ min.	1 min.	2 min.	1½ min.	1½ min.	1½ min.	1½ min.	1 min.	1 min.
Coagulation time	4 min.	....	....	5 min.	7 min.	....	....	....	....	....	....	....	....	....
Tourniquet test	Positive	....	....	Positive	Slightly positive 2 petechiae	....	....	Negative	....	....	....	Negative	Negative	Negative
Clot retraction	Absent after 6 hrs.	....	Absent after 24 hrs.	Absent 4 hrs., v. slight 24 hrs.	Positive in 1½ hrs.	....	....	Positive in 1 hr.	....	....	....	....	Positive in 1 hr.	Positive in 1 hr.

tomy was followed by a postoperative pneumonia, after which the child made an uninterrupted recovery.

Not only the change in the clinical condition but the immediate and later changes in the hematologic findings were of great interest. Before operation all the laboratory findings characteristic of this disease were present, the bleeding time was twenty minutes (normal from one to three minutes); the coagulation time was four minutes (normal); clot retraction was absent even after six hours (normal in one hour); the capillary resistance test of Hess was present, petechiae rapidly appearing on the skin of the forearm when the sphygmomanometer cuff was applied to the arm; the blood platelets were reduced as low as 2,000 per millimeter (normal 250,000). Curiously enough, in spite of the continued hemorrhages, there was present only a mild anemia, the red cells being normal in number, the hemoglobin being 60 per cent. One hour after the spleen had been removed the bleeding time had decreased to five minutes, twenty-four hours later it had decreased to one minute. It remained at from one to one and one-half minutes, from that time on, being still the same five months after operation. Clot retraction appeared twenty-four hours after splenectomy and has been present ever since. The tourniquet test was negative one week after operation and has remained so. The blood platelets counts were as follows: Before operation, 2,000, one hour after operation, 42,000, twenty-four hours postoperative, 80,000, on the fourth day, 220,000, after three weeks, 100,000, after three months, 90,000, the hemoglobin which was 60 per cent. before operation, rose to 85 per cent., at which it has remained. The bleeding stopped completely and the patient has been perfectly well since the operation five months ago.

ACUTE PELVIC ABSCESS IN CHILDREN *

REPORT OF TWO CASES RUPTURING INTO THE VAGINA

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A review of pediatrics and surgical literature indicates that acute pelvic abscess in infants rupturing through the vagina is rare. The following two cases were observed.

REPORT OF CASES

Case 1.—A girl, aged 2 months, was the fourth child, of normal birth, and breast fed. The patient had been healthy from birth except for frequent stools. One day suddenly and without apparent cause she became fretful and developed a temperature of 103. Forty-eight hours later the mother noticed a profuse, greenish vaginal discharge, without odor, which persisted for about five days. With the appearance of the discharge the temperature became normal and the child was apparently well. About six weeks later, she again became fretful and feverish. With the appearance of a similar vaginal discharge she apparently felt well. After another interval of three months, during which time the child gained in weight normally and seemed to be in perfect health, the cycle of fever and discharge, followed by relief of symptoms, appeared. The discharge this time was much less copious, persisting, however, for about six days. Physical examination was always negative for any pathologic findings, except that during the time of the discharge pressure exerted deep in the pelvis behind the bladder brought an increase in the vaginal flow and at times even a spurt of pus from the vagina could be produced. No abdominal or pelvic mass was palpable. The vaginal discharge was definitely a greenish-yellow, odorless pus. No gonococci were found but staphylococci and pyocyaneus were present. Rectal examination was negative. The diagnosis was pelvic abscess of unknown origin, which ruptured spontaneously into the genital tract. The child is now 10 months old and apparently well.

Case 2.—A girl, aged 9 months, entered the service of Dr. Julius H. Hess on March 23, 1922, with a history of restlessness and elevation of temperature for one week. The patient cried considerably. The temperature at one time was 105. The right ear drum had been incised four days previous to entrance.

Physical examination disclosed a very irritable baby. There was a purulent discharge from the right ear and the left ear drum was bulging. The throat was markedly injected. There were no other abnormal findings. The white blood count was 23,000, of which 56 per cent. were neutrophils, 32 per cent. small mononuclears and 12 per cent. large mononuclears. Hemoglobin was 70 per cent. and red blood count 3,800,000. The left ear drum was incised. Both ears discharged freely, but the temperature persisted, with daily rises as high as 103.

April 19, the parents insisted on taking the patient home. At the time of release the baby had a rectal temperature of 106.6, white blood count 15,000,

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* Received for publication, Jan. 21, 1924.

the ears were discharging only slightly and the glands of the neck were not enlarged. It was difficult at this time to account for the temperature A few days later the child became worse. The parents called in their family physician, Dr. Lebowitz, to whom we are indebted for the subsequent history. The child seemed ill, and apparently in pain, the right thigh was held flexed on the abdomen and efforts to extend the limb were painful. The leg was edematous. A roentgen-ray examination was made of the right hip and at the same time the abdomen was fluoroscoped. A mass was seen in the right flank. During the manipulations, the right thigh was slightly extended and suddenly a gush of pus issued from the vagina. Prompt and complete recovery followed. There has been no recurrence to date.

Here again we were dealing with a pelvic abscess of unknown origin, which ruptured spontaneously into the vagina.

Griffith says most frequent forms of localized peritonitis is that associated with appendicitis. Its presence is also to be suspected whenever a child with gonorrheal vulvovaginitis suddenly develops fever with abdominal pain, tenderness and distention. He had seen this in but two instances.

Stoos [1] states that the etiology of localized peritonitis is somewhat different in infants than in older children. Appendicitis, the most frequent cause in children over 2 years, is rare in the first year of life, as is also encapsulated pneumococcus peritonitis.

Hertzler [2] states that localized pneumococcic peritonitis is more frequent in girls, occurring in forty-five out of fifty-two cases. Only five cases of ruptured pneumococcic peritonitis are reported and those through the umbilicus.

Nothnagel,[3] in speaking of appendicitis and spontaneous cures, states that perforation may occur into the ascending colon, ileum, rectum and even into the duodenum. Perforation into the bladder is rare and into the vagina still rarer. Perforation into the uterine cavity, reported by Langheld, is a pathologic curiosity.

Ashby speaks of general and localized peritonitis development from infected retroperitoneal glands which break down. These we feel may be the cause in our cases.

McCartney [4] brings out the fact experimentally in monkeys, that pneumococcic peritonitis arises from vaginal infections, as they occur in girls, and usually not before the age of 3 years. These again are different from our cases, ours being in infants under 1 year, and rupturing spontaneously.

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[1] Stoos, U.: Pflaundler Schlossmann, Philadelphia, J. B. Lippincott Company, 1912, p. 251.

[2] Hertzler: The Peritoneum, St. Louis, C. V. Mosby Company, 1919, p. 169.

[3] Nothnagel: Diseases of the Peritoneum, Philadelphia, W. B. Saunders Company, 1905, p. 868.

[4] McCartney, J. E.: Pathogenesis of Primary Pneumococcal Peritonitis, Brit. J. Pathol. & Bacteriol. **26**:507 (Oct.) 1923.

In connection with these cases the following two cases might be of interest in explaining the etiology of some of these abscesses.

REPORT OF CASES

Case 1.—A girl, aged 5 years, was brought into the Sarah Morris Hospital on the service of Dr. Hess because of abdominal pain, painful urination and poor appetite. The patient was apparently well until two weeks previous to admission to the hospital, when she commenced to complain of painful urination. There was a slight frequency but no blood or gravel was noticed in the urine. Nausea was present at the onset but later subsided. The condition became progressively worse and was accompanied by a daily rise in temperature. One week previous to admission the child complained of a severe abdominal colic and pointed to the left lower quadrant. The bowels were regular but the appetite was very poor. The patient had scarlet fever at the age of 2, and measles at 3 years of age. The family history was negative for tuberculosis.

Physical Examination.—At the time of admission examination revealed a well-developed girl with flushed face, lying flat in bed with the right thigh flexed on the abdomen. The abdomen was tense all over but not distended. Rigidity and tenderness were present on both sides but most marked in the lower right abdominal quadrant. The temperature was 100.4, respiration 32. White blood count was 18,000, with 80 per cent. polymorphonuclears. The urine showed a faint trace of albumin with an occasional white blood cell. A definite mass was palpable just below the umbilicus, and a diagnosis of acute appendicitis with probable abscess formation was made and immediate operation advised.

At operation, the following conditions were noted: There was no free fluid in the abdomen. The appendix was slightly injected but clearly was not the cause of the symptoms. The mass, which had been noted previous to operation, could be definitely felt extending out of the pelvis from about the level of the promontory of the sacrum up to the abdominal wall. It was walled off by firm adhesions. A stab wound was made through the midline of the abdominal wall and a thick creamy, odorless pus flowed out, from which staphylococci were cultured. A finger was then introduced into the abscess cavity and a few partitions broken down. The first incision, which had been walled off, was closed and the abscess drained through the stab wound. The internal genitalia, on rectal examination after operation, appeared normal.

The patient made an uneventful recovery. The wound stopped draining in about two weeks, and she was discharged about a week later.

After the operation, careful roentgen-ray examinations were made of the spine and pelvis but no signs of bone destruction were noted. The diagnosis was pelvic abscess of unknown origin.

Case 2.—A boy, aged 3 years, was admitted to the Sarah Morris Hospital, July 24, 1921, with a history of fever, soreness on the right side of abdomen and a "sore" mouth.

Twenty-two days previous to entrance, the patient awakened in the morning as usual, but was unable to stand because of pain in the right limb. He was able to move the limb voluntarily, however. The condition seemed to progress so that for five days before admission he was unable to stand at all. He had an elevation of temperature for several days, but the exact temperature was not taken. For four weeks he had "sores" in the mouth. The bowels were regular and the appetite was good up to the day before entrance. He had had no diarrhea or vomiting. There had been no previous illness, and the family history was negative.

Physical Examination.—The patient was a well-developed child, who held the right lower extremity in a flexed position. He could not extend it without pain. There was a mass in the lower abdomen on the right side, extending down to above the hip joint and laterally in the flanks. Increased muscle rigidity and tenderness were present. On rectal examination no mass was palpable.

Roentgen-ray examination of the right hip was negative. The temperature was 99.6 rectal, pulse 120. White blood count was 27,000, of which 65 per cent. were neutrophils, 30 per cent. small mononuclears, 4 per cent. large mononuclears and 1 per cent. transitionals. The urine was negative. The Pirquet and Wassermann tests were negative.

An exploratory laparotomy was performed. The appendix was normal. A large, boggy retroperitoneal mass was palpated in the right lower quadrant. There was no definite fluctuation. The peritoneum was closed and the mass exposed by elevating the peritoneum. The mass was found to be composed of large swollen retroperitoneal glands. Inasmuch as infection was definitely present, no attempt was made to excise a piece for microscopic study. A small gutta-percha drain was left in the wound, and for a week there was a slight serous discharge.

The patient made an uneventful recovery, and went home at the end of two weeks, at which time the glands had disappeared and the child walked normally.

The probable etiology was the same as that of the stomatitis, which was present for four weeks previous to admission.

CONCLUSIONS

Three cases of acute pelvic abscess formation are reported, with relief of symptoms in each case after drainage. In the first two, this occurred spontaneously through the vagina and in the third case artificially by operation. In the third case the cause of the abscess was proved to be not the appendix, and it probably did not originate from the internal genitalia, which were palpated and found to be normal. The abscess possibly originated from the retroperitoneal structures and was presumably of glandular origin. The frequent association of abdominal pain with throat conditions in childhood, recently brought to our attention by Brennemann,[5] is known to us. Some pelvic abscesses might be from just such infections involving the lymph glands which break down. We are absolutely at a loss to explain the source otherwise. They were not appendiceal abscesses. These, of course, may rupture spontaneously but they almost invariably rupture into the bowel. A spondylitis might give rise to a pelvic abscess but no signs or symptoms pointing to spinal origin were present, nor in such cases would the patients be apt to recover spontaneously. The fact that all three cases occurred in female patients, and that in two there was a discharge of pus from the vagina, might point to the genitalia as the source. Pyosalpinx has been known to occur in infants, and must be considered as a possible etiologic factor.

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[5] Brennemann, Joseph: The Abdominal Pain of Throat Infections, Am. J. Dis. Child. **22**:493 (Nov.) 1921.

THE ESTIMATION OF THE VOLUME OF BLOOD IN NORMAL INFANTS AND IN INFANTS WITH SEVERE MALNUTRITION *

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No study on fluid regulation in the body can be complete without some knowledge of the total amount of circulating fluid. Because of the large quantities of blood hitherto necessary to estimate the blood volume, few determinations have been made in infants. It was primarily with the purpose of obtaining more data on the subject that this investigation was undertaken.

The method used for estimating the volume of blood was a micromodification of the method of Keith, Rowntree, and Geraghty [1] as improved by Hooper, Smith, Belt and Whipple.[2] A known amount of a nontoxic, slowly diffusible dye is injected into a vein, is allowed to circulate for a few minutes and a specimen of blood withdrawn. By determining the concentration of the dye in the plasma, the plasma volume may be calculated. The total blood volume may be computed from the hematocrit reading.

In normal adults the total volume of blood is about 9 per cent. of the body weight, and the plasma volume about 5 per cent.[1] In normal infants Lucas and Dearing [3] found that the values were higher and varied much more widely than in adults. According to these observers, in the new-born the volume of blood varies from 10.7 to 19.5 per cent. of the body weight, averaging 14.7. The plasma volume varies from 4.2 to 7.7 per cent. of the body weight, averaging 5.9. In older infants the blood volume ranges from 9.0 to 12.6 per cent. of the body weight averaging 11.0. The plasma volume varies from 5.7 to 7.8 per cent. of the body weight, averaging 6.7.

Marriott and Perkins [4] determined the volume of blood in normal infants and in infants with marasmus. They found that in seven

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* Received for publication, Jan. 23, 1924.

* From the pediatric service, New York Nursery and Child's Hospital, and the Department of Pediatrics, Cornell University Medical College.

[1] Keith, N. M.; Rowntree, L. G., and Geraghty, J. T.: A Method for the Determination of Plasma and Blood Volume, Arch. Int. Med. **16**:547 (Oct.) 1915.

[2] Hooper, C. W.; Smith, H. P.; Belt, A. E., and Whipple, G. H.: Experimental Control of a Dye Blood Volume Method, Am. J. Physiol. **51**:205 (March) 1920.

[3] Lucas, W. P., and Dearing, B. F.: Blood Volume in Infants Estimated by the Vital Dye Method, Am. J. Dis. Child. **21**:96 (Jan.) 1921.

[4] Marriott, W. M., and Perkins, J. F. (quoted by Marriott): Some Phases of the Pathology of Nutrition in Infancy, Harvey Lectures, 1920-1921, p. 121.

normal infants the volume of blood varied from 8.0 to 10.8 per cent. of the body weight. In eleven infants with marasmus the values ranged from 4.0 to 10.4 per cent. of the body weight. They state that the higher values were obtained in infants who might be considered as convalescing from the marasmus. They conclude that the volume of blood in infants with marasmus is lower that in normal infants.

PROCEDURE AND METHODS

The blood volume was determined in a group of normal infants and infants with severe malnutrition. Estimations of the serum protein concentration and hemoglobin percentage were made at the same time.

Determinations were made from three to four hours after a feeding. To avoid diurnal variations the blood specimens were always taken at the same time of the day (between 1 and 2 p. m.). Specimens for hemoglobin and serum protein estimations were obtained immediately before the dye was injected. Hemoglobin was determined by the carbon monoxid method of Palmer.[5] The serum protein concentration was determined with the Abbe refractometer. The technic used was similar to that described in previous papers.[6] The calculations were made according to Reiss.[7]

The following micromodification of the dye method of Keith, Rowntree and Geraghty[1] was used to determine the volume of blood: A 1.5 per cent. solution of brilliant vital red in saline was prepared. This solution was sterilized before each set of determinations. Two cubic centimeters of blood were drawn into a dry syringe and delivered into a heavy walled hematocrit tube, 12.5 cm. in length and 0.6 cm. in diameter. The graduated tubes were calibrated in divisions of 0.04 c.c. and contained 0.4 c.c. of 1.6 per cent. sodium oxalate solution to prevent clotting. The oxalate and blood were mixed by inverting. The plasma obtained in this way was later used in the preparation of the standard.

Without removing the needle from the vein, 1 c.c. of dye, prepared in the manner described above, was injected.[8] Four minutes later a fresh needle was introduced and 2 c.c. of blood again withdrawn. The blood obtained in this way was delivered into a tube similar to the first and also containing 0.4 c.c. of sodium oxalate solution.

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5. Palmer, W. W.: The Colorimeter Determination of Hemoglobin, J. Biol. Chem. **33**:119 (Jan.) 1918.

6. Bakwin, H.: Dehydration in New-Borns, Am. J. Dis. Child. **24**:497 (Dec.) 1922.

7. Reiss, E.: Die refraktometrischen Untersuchungen und ihre Ergebnisse für die Physiologie und Pathologie des Menschen, Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

8. The amount of dye used for injection may be varied according to the weight of the subject. The variation in the weight of the babies studied was comparatively small, and we therefore used 1 c.c. except in infants under 3 kg. in whom 0.5 c.c. was used.

Both tubes were then centrifuged for twenty minutes at 1,500 revolutions per minute and hematocrit readings made in the tubes. The supernatant fluid (plasma and oxalate solution) was pipetted off into clean test tubes. One cubic centimeter of the dye-stained plasma oxalate mixture was added to 2 c.c. of normal saline and matched in a colorimeter (using microcups and microplungers) against the standard mixture. The standard mixture consisted of 1 c.c. of saline, 1 c.c. of plasma oxalate solution obtained before the dye was injected and 1 c.c. of dilute dye solution.[9] The dilute dye solution was prepared by making up 1 c.c. of 1.5 per cent. dye solution to 400 c.c. with saline. This was prepared before each set of determinations.

The calculations were as follows:

$$\text{Plasma volume} = \frac{R}{15} \times 400 \times \frac{P - 0.4}{P} \times D$$

$$\text{Blood volume} = \frac{\text{plasma volume}}{\text{plasma per cent.}} \times 100$$

Corpuscular volume = blood volume minus plasma volume

where

R = colorimeter reading with the standard at 15.

P = amount of dye-stained plasma oxalate solution in the hematocrit tube.

D = c.c. of dye injected.

$$\text{Plasma per cent.} = \frac{P - 0.4}{\text{Total amount of fluid in tube minus } 0.4} \times 100$$

This is probably as accurate as the original method, since the errors due to measuring the smaller amounts of fluid are well within the limits of error inherent in the method.[10]

The longitudinal sinus was used in all the determinations. A short beveled, 20 gage needle, 6 mm. in length, proved entirely satisfactory.

All the babies used in this study were artificially fed. It was not possible to obtain a large series of strictly normal babies. The "normal" babies were healthy in the sense that they were not suffering from any acute illness. Some of them were slightly underweight. None of the babies had fever.

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[9] In the experiments of Lucas and Dearing,[3] sodium oxalate solution was added to the tube containing the blood obtained before the dye was injected but not to the second tube. The actual amount of plasma in their standard tubes was therefore from 25 to 40 per cent. less than in the "unknown" tube. We have found that even small discrepancies in the actual amount of plasma added causes difficulty in the colorimeter reading. The plasma of the new-born is often high colored. In older infants turbid serums are not infrequently encountered.

[10] The exact manner in which the dye is removed from the body is unknown. Keith, Rowntree and Geraghty, using vital red, found small amounts in the urine. With the specimen used in these experiments (brilliant vital red) the urine was always negative. In the feces, however, dye was regularly present, in one instance as early as ten hours after the injection and as late as eleven days afterward.

RESULTS

Repeated determinations of the blood, plasma and corpuscular volumes on the same patient were made in sixteen instances (Table 1). Two of the infants were markedly underweight (Cases 537, 542). Two others were anemic (Cases 548, 549). The rest of the babies were fairly normal.

TABLE 1.—*The Results of Repeated Determinations of the Blood Volume, Etc., in Infants.*

			Total Volume			Volume per Kg. Body Weight				
Case	Age, Months	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
504	¾	3.47	344	204	140	99	59	40	12.9	—
	1½	3.46	334	214	120	97	62	35	11.2	—
505	1	2.76	353	198	155	128	71	57	14.3	—
	1½	2.93	281	178	103	96	61	35	11.7	—
	3½	3.93	372	243	129	94	61	33	—	—
506	1½	2.78	413	185	228	148	66	82	16.8	—
	1¾	3.04	360	190	170	117	63	54	13.8	4.90
513	2	3.72	401	272	129	108	69	39	11.7	5.49
	3	4.20	377	242	135	90	58	32	10.4	—
532	2	2.79	326	210	116	117	75	42	9.5	5.31
	2½	2.82	364	236	128	129	84	45	11.2	—
510	2	3.47	325	228	97	94	66	28	9.9	5.31
	4	3.58	403	258	145	113	72	41	12.9	—
537	3	2.93	334	216	118	115	74	41	10.3	5.95
	3½	2.93	347	218	129	118	74	44	11.2	—
536	3	2.87	353	242	111	126	85	41	—	7.11
	3½	2.98	366	248	118	123	83	40	9.0	6.53
	3¾	3.38	396	250	146	117	74	43	12.6	6.53
519	3½	3.90	434	270	164	112	69	43	12.5	7.11
	3¾	4.32	452	282	170	105	65	40	—	—
517	3½	4.35	437	284	153	101	65	36	10.1	—
	4	4.52	403	272	131	89	60	29	9.7	5.84
523	5	5.48	457	290	167	83	53	30	10.5	—
	5½	5.77	524	344	180	91	60	31	10.6	6.17
	6	6.03	517	326	191	86	54	32	—	—
	6½	6.17	575	359	216	93	58	35	10.7	6.59
542	5	2.90	228	161	67	79	56	23	9.2	5.78
	5½	2.90	276	185	91	95	64	31	9.6	5.89
	6	3.04	294	206	88	97	68	29	10.1	6.24
	7	3.41	342	238	104	100	70	30	9.8	—
524	5½	5.12	479	303	176	94	59	35	11.8	—
	5¾	4.97	520	327	193	105	66	39	12.7	—
546	6½	4.67	444	302	142	95	65	30	8.6	7.79
	7½	4.66	483	314	171	104	67	37	10.7	7.93
	7¾	4.88	503	326	177	103	67	36	9.7	7.56
548	7	3.41	300	225	75	88	66	22	7.2	—
	7½	3.54	422	308	114	115	85	30	8.1	—
549	9	4.80	446	334	112	93	70	23	5.2	6.87
	9½	4.83	467	356	111	97	74	23	6.1	7.17

In the three infants under 8 weeks of age on whom repeated determinations were made (Cases 504, 505, 506) a drop in the absolute volume of corpuscles occurred. In Case 505, despite the fact that the baby gained 170 gm. in two weeks, the volume of red cells fell from 155 c.c. to 103 c.c. In Case 506, similarly, though the baby gained 250 gm. in weight during the week intervening between the two determinations, the volume of red cells fell from 228 c.c. to 170 c.c. In the only infant under 8 weeks of age on whom Lucas and Dearing made repeated determinations (their Table 4, Case B. O.) a similar drop in the absolute volume of red cells from 175 c.c. to 134 c.c. occurred.

The volume of plasma in our cases showed little change during this period of life. It increased slightly in two cases and fell slightly in the third. In the patient studied by Lucas and Dearing there was a considerable increase in the plasma volume between the fifteenth and fiftieth days.

In all four infants the fall in red cell volume was accompanied by a drop in the hemoglobin percentage. It is known that the red cell count during this period falls rapidly. These results indicate that the fall in the hemoglobin percentage and red cell count during the first weeks of life is owing to an actual reduction in the number of circulating corpuscles and not to an increase in the plasma volume.

After the first weeks of life the volume of plasma and corpuscles increases steadily. It is interesting to note that this usually proceeds even though no significant gain in weight occurs (Table 1, Cases 532, 537, 542, 524, 546, 549).

The Relation Between the Volume of Blood and the Body Weight in Normal Infants.—A résumé of the results of estimations of the volume of blood, plasma and red cells together with other data is given in Table 2. In Charts 1, 2 and 3 the blood, plasma and corpuscular volumes per kilogram of body weight, respectively, are graphically represented in relation to age. The dots represent individual determinations. The continuous lines in Charts 1, 3, 4 and 6 represent the average at different ages as obtained by the method of least squares.

The volume of blood per kilogram of body weight in normal infants varies from 71 c.c. to 148 c.c., averaging 101 c.c. The values obtained, like those of Lucas and Dearing, are not only higher than in adults but they vary more widely. It is of interest that the highest figures were obtained during the new-born period (Chart 1). There is a gradual fall as the age increases but at 7 months the blood volume is still relatively higher than in adults. The variations in results are also more marked during the new-born period than later in infancy.

That the decrease in the amount of blood per kilogram of body weight as the age increases is due to a diminution in the volume of red cells is apparent from Charts 2 and 3. The volume of red cells is relatively high during the first weeks of life. It falls, abruptly at first, more gradually later, the curve for the corpuscular volume running in a general way parallel to that of the total blood volume.

The volume of plasma per kilogram of body weight (Chart 2) shows wide variations (38 c.c. to 72 c.c., averaging 61 c.c. per kilogram of body weight) particularly during the new-born period. This is in marked contrast to the relative constancy of the plasma volume in adults.[11] Recent studies tend to show that, in adults of the same nutritional condition, despite wide variations in the volume of corpuscles, the plasma volume remains fairly constant. Bock [11] points out that even in such widely different conditions as polycythemia and pernicious anemia, though the red cell volume varies greatly, the plasma volume remains relatively unchanged.

Table 2.—*The Blood Volume in Normal Infants*

			Total Volume			Volume per Kg. Body Weight				
Case	Age	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
500	12 days	2.40	253	91	162	105	38	67	19.4	—
501	2 wks.	3.04	358	222	136	118	73	45	12.8	5.49
502	2 wks.	2.84	304	152	152	107	54	53	—	6.01
503	3 wks.	3.60	402	186	216	113	52	61	18.4	5.78
504	3 wks.	3.47	344	204	140	99	59	40	12.9	—
505	1 mo.	2.76	353	198	155	128	71	57	14.3	—
518	5 wks.	2.78	294	161	133	106	57	48	13.8	5.14
504	5 wks.	3.39	386	211	175	114	62	52	13.3	5.78
504	5 wks.	3.46	334	214	120	97	62	35	13.1	—
506	6 wks.	2.79	413	185	228	148	66	82	16.8	—
505	6 wks.	2.93	281	178	103	96	61	35	11.7	—
509	6 wks.	3.64	372	244	128	102	67	35	10.3	6.30
506	7 wks.	3.04	360	190	170	117	62	54	13.8	4.90
510	2 mos.	3.47	325	228	97	94	66	28	9.9	5.34
511	2 mos.	4.85	448	282	166	93	58	34	11.3	5.66
512	2 mos.	4.09	299	206	93	73	50	23	—	—
513	2 mos.	3.72	401	272	129	108	69	39	11.7	5.49
513	3 mos.	4.20	377	242	135	90	58	32	10.4	—
514	3 mos.	3.42	368	236	132	108	69	39	12.7	5.37
515	3 mos.	4.83	453	310	143	94	64	30	10.4	5.95
517	3 mos.	4.35	437	284	153	101	65	35	10.1	6.70
505	3 mos.	3.98	372	243	129	94	61	33	—	—
519	3 mos.	3.90	434	270	164	112	69	43	12.5	7.11
519	4 mos.	4.32	452	282	170	105	65	40	—	—
510	4 mos.	3.58	403	258	145	113	72	41	11.4	—
517	4 mos.	4.52	403	272	131	89	60	29	9.7	5.84
521	5 mos.	5.38	515	320	195	96	60	36	10.6	7.11
575	5 mos.	4.99	478	303	175	96	61	35	12.8	5.37
523	5 mos.	5.48	457	290	167	83	53	31	10.5	—
523	5½ mos.	5.77	524	344	180	91	60	31	10.6	6.07
524	5½ mos.	5.12	479	303	176	94	59	35	11.8	....
524	5¾ mos.	4.97	520	327	193	105	66	39	12.7	....
523	6 mos.	6.03	517	326	191	86	54	32	....	....
523	6½ mos.	6.17	575	359	216	93	58	35	10.7	6.59
525	7 mos.	5.62	408	270	138	71	48	23	—	6.65
528	10 mos.	6.53	534	320	114	82	49	33	9.4	—

It is probable that these wide variations in the relation between plasma volume and body weight in infants are due, in part at least, to the fact that the daily up and down fluctuations in the weight curve of an artificially fed infant do not represent the true weight of the baby but are due to changes in the water content of the tissues. Freund [12] studied the nitrogen and chlorin balance in a series of artificially fed infants and found that during days of rapid weight gain the nitrogen retention was sufficient to account for only a small part of the gain.

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[11] Bock, A. V.: The Constancy of the Volume of the Blood Plasma, Arch. Int. Med. **27**:83 (Jan.) 1921.

[12] Freund, W.: Wasser und Salze in ihren Beziehungen zu den Körpergewichtsschwankungen der Säuglinge, Jahrb. f. Kinderh. **59**:421, 1904.

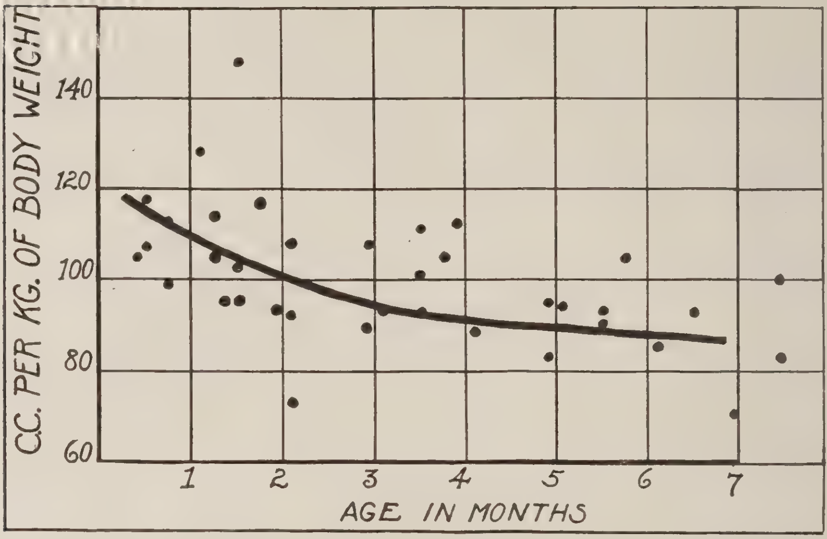

Chart 1.—The volume of blood per kilogram of body weight in relation to age in normal infants.

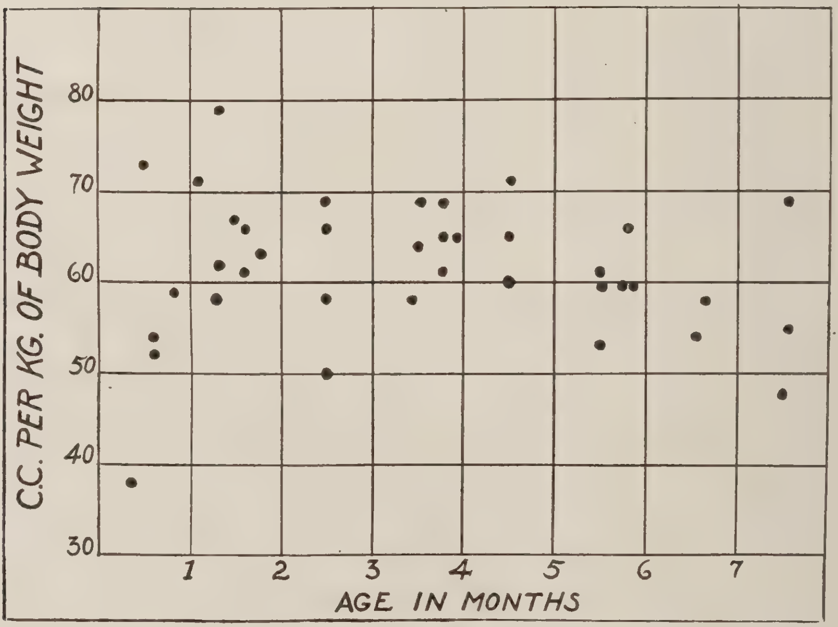

Chart 2.—The volume of plasma per kilogram of body weight in relation to age in normal infants.

That the major part of the weight increase was due to water retention was shown by a marked diminution in the elimination of chlorid and alkali salts. Moreover it has been found [13] that rapid weight increases in artificially fed infants are not accompanied by an increase in the water content of the plasma, thus indicating that the increased amount of fluid is held in the tissues and does not enter the blood.

Table 3.—*The Blood Volume in Infants with Severe Malnutrition*

			Total Volume			Volume per Kg. Body Weight				
Case	Age, Months	Weight, Kg.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Blood, C.c.	Plasma, C.c.	Corpuscles, C.c.	Hemoglobin, Gm. per 100 C.c.	Serum Protein, per Cent.
529	2	2.61	282	171	111	108	66	42	6.44	6.53
530	2	2.99	276	182	94	92	61	31	10.0	6.24
531	2	2.80	235	153	82	84	54	30	—	—
532	2	2.79	326	210	116	117	75	42	9.53	5.31
532	2½	2.82	364	236	128	129	84	45	11.2	—
533	2½	3.04	330	244	86	109	81	28	8.5	5.25
534	3	3.18	325	214	111	105	67	38	10.7	5.43
536	3	2.87	353	242	111	126	85	41	—	7.11
537	3	2.93	334	216	118	115	74	41	10.3	5.95
537	3½	2.93	347	218	129	118	74	44	11.2	—
538	3½	3.97	314	204	110	79	51	28	9.6	5.95
536	3½	2.98	366	248	118	123	83	40	9.0	6.53
536	3¾	3.38	396	250	146	117	74	43	12.6	6.53
576	4	3.10	308	209	99	99	67	32	10.4	—
577	4	4.00	387	255	132	97	64	33	11.38	5.89
539	4	4.00	468	312	156	117	78	39	11.1	6.24
540	4½	4.80	405	272	133	84	57	27	10.0	7.11
541	5	4.00	490	313	177	123	79	44	10.7	6.36
542	5	2.90	228	161	67	79	56	23	9.2	5.78
542	5½	2.90	276	185	91	95	64	31	9.6	5.89
542	6	3.04	294	206	88	97	68	28	10.1	6.24
543	6	3.64	354	225	128	97	62	35	10.2	7.52
544	6	3.58	366	250	116	102	70	32	12.8	5.37
545	6	4.54	401	269	132	88	59	29	9.4	6.36
546	6½	4.67	444	302	142	95	65	30	8.6	7.79
547	7	4.60	390	252	138	84	55	29	7.87	4.85
526	7	4.09	341	224	117	84	55	28	10.4	—
542	7	3.41	342	238	104	100	70	30	9.8	—
548	7	3.41	300	225	75	88	66	22	7.17	—
548	7½	3.64	422	308	114	115	85	30	8.05	—
549	7½	4.35	437	298	139	101	69	31	9.1	6.81
546	7½	4.66	483	314	169	104	67	37	10.7	7.93
546	7¾	4.88	503	326	177	103	67	36	9.7	7.56
567	9	4.30	493	306	187	115	71	44	11.1	7.05
559	9	4.80	445	334	111	93	70	23	5.2	6.87
559	9½	4.83	467	356	111	97	74	23	6.1	7.17
550	12	5.10	553	338	215	108	66	42	9.7	7.11
551	14	3.50	309	221	88	88	63	25	7.9	4.07
552	14½	3.05	325	224	101	107	74	33	—	6.12
553	15	6.24	630	420	110	101	67	34	—	7.81

The Volume of Blood in Infants with Severe Malnutrition.—A résumé of the results in infants with severe malnutrition is given in Table 3. In Charts 4, 5 and 6 the blood, plasma and corpuscular volumes, respectively, per kilogram of body weight are represented according to age. The crosses indicate individual determinations in marantic babies. The dots in Chart 5 represent individual determinations in normal babies and are inserted for comparison. The heavy continuous lines in Charts 4 and 6 are transcribed from Charts 1 and 3

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[13] Bakwin, H.: The Water Content of Infants' Blood During Periods of Rapid Increase in Weight, Am. J. Dis. Child. **25:**406 (May) 1923.

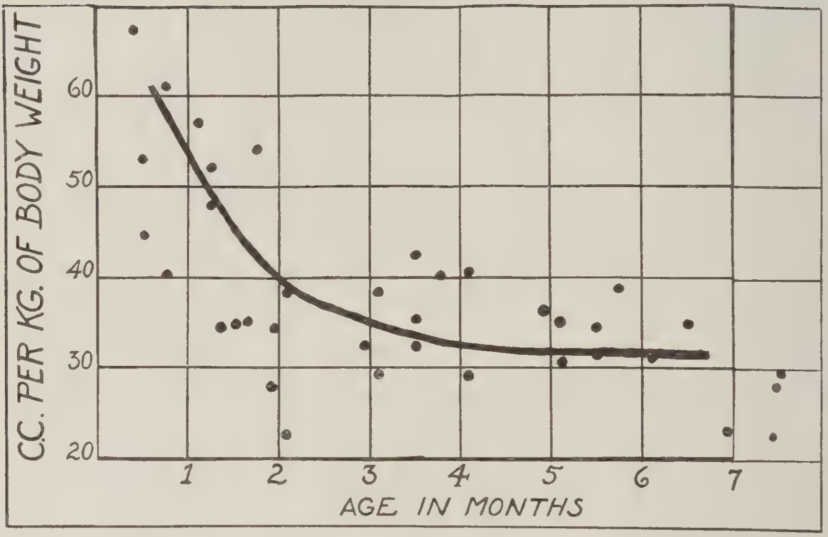

Chart 3.—The volume of red cells per kilogram of body weight in relation to age in normal infants.

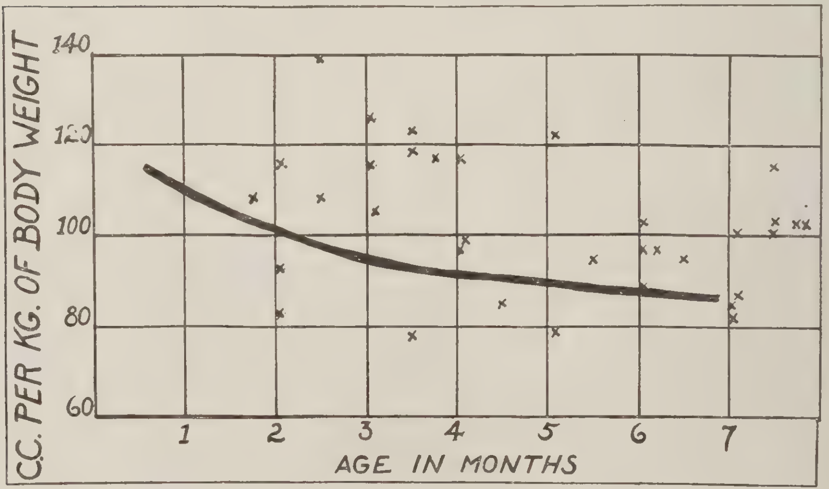

Chart 4.—The volume of blood per kilogram of body weight in relation to age in infants with severe malnutrition.

and represent the averages for the blood and red cell volumes per kilogram of body weight at different ages as obtained by the method of least squares.

The average value obtained for the infants with severe malnutrition varies little from the normal average (103 c.c. of blood per kilogram of body weight for infants with marasmus, 101 c.c. for normal infants). However, since, in computing the normal average, the values obtained in infants during the first weeks of life when the blood volume is high were included, the averages for normal and marantic infants are not directly comparable. Most of the normal babies were under 4 months, whereas most of the marantic infants were past this age. For the same age period the blood volume in infants with marasmus is relatively higher than in normal infants (Chart 4). This is true in spite of the fact that most of the infants with marasmus were more or less anemic (hemoglobin under 10 gm. per hundred cubic centimeters of blood), a factor which would tend to lower their blood volume.

The plasma volume in marantic infants is relatively higher than in normal infants. The average value for the plasma volume in infants with marasmus is 69 c.c. per kilogram of body weight, for normal infants 61 c.c.

The Relation Between the Volume of Blood and the Body Surface in Infants.—According to Dreyer and Ray [14] the volume of blood in mammals is proportional to the body surface and not to the body weight. They believe that the practice of expressing the blood volume in percentage of body weight is misleading, particularly when individuals of different nutritional conditions are compared. Since adipose tissue is comparatively nonvascular, thin individuals of the same length and muscular development should have a larger blood volume in relation to the body weight than fat individuals. The bodies of the infants with malnutrition obviously contained less fat than normal babies, and one would therefore expect them to have a higher blood volume in relation to body weight than normal infants.

The blood volume was computed in relation to body surface [15] in nineteen cases. Whereas in adults the amount of blood per square meter of body surface averages 3.12 liters,[16] the average value for infants is 1.7 liters. Though the blood volume in an infant, therefore, is large in proportion to the body weight it is much smaller than the adult in relation to body surface.

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[14] Dreyer, G., and Ray, W.: Phil. Tr. Roy. Soc. London, **201**:133, 1910.

[15] Dubois, D., and Dubois, E. F.: A Formula to Estimate the Approximate Surface Area if Height and Weight be Known, Arch. Int. Med. **17**:863 (June) 1916.

[16] Keith, N. M.: The Total Circulating Volume of Blood and Plasma in Cases of Chronic Anemia and Leukemia, Am. J. M. Sc. **165**:174 (Feb.) 1923.

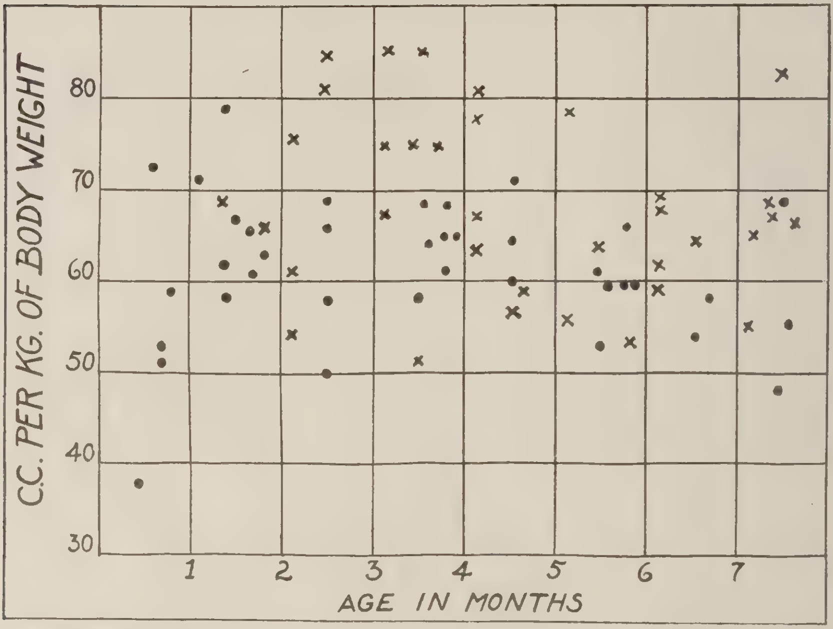

Chart 5.—The volume of plasma per kilogram of body weight in relation to age in infants with severe malnutrition.

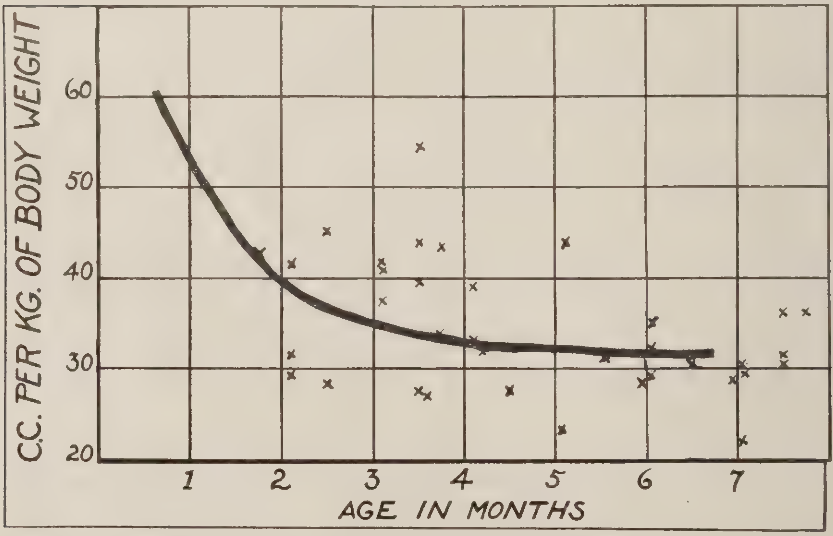

Chart 6.—The volume of red cells per kilogram of body weight in relation to age in infants with severe malnutrition.

The Relation Between the Serum Protein Per Cent. and the Plasma Volume.—No relation was found between the plasma volume per kilogram of body weight and the serum protein per cent.

SUMMARY AND CONCLUSIONS

1. A micromodification of the dye method of Keith, Rowntree, and Geraghty has been described, by which the volume of blood can be determined with 4 c.c. of blood.

2. At birth, the corpuscular volume is relatively high. It falls rapidly during the first weeks of life, so that the absolute volume of red cells is less at 8 weeks of age than at birth.

3. The volume of blood and plasma in infants is higher in relation to the body weight and varies more widely than in adults. The average value for the blood volume is 101 c.c. per kilogram of body wieght. The average value for the plasma volume is 61 c.c. per kilogram of body weight.

4. The volume of blood and plasma in marantic infants is higher than in normal infants.

5. The volume of blood per unit of body surface in infants is much smaller than in adults (1.7 liters per square meter for infants, 3.12 liters for adults).

A COMPARISON OF THE METABOLISM OF SOME MINERAL CONSTITUENTS OF COW'S MILK AND OF BREAST MILK IN THE SAME INFANT *

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It is an established fact that the mineral constituents of cow's milk are not so well utilized by infants as are those of breast milk. This fact, however, seems to have been based largely on investigations in which different infants were employed as subjects for the experiments on the two kinds of milk. It is a matter of surprise, on going through the literature, to see how little has been written regarding the mineral metabolism in the same infant fed on the two kinds of milk. Since the constitution of normal people is known to vary to a certain extent with different persons, the difference in the utilization of the mineral constituents of the two milks may be owing not only to the nature of the milk, but to the constitutional differences of the individual infants. In order to determine whether there is any difference in the utilization of mineral constituents of the two milks by the same infant, a series of metabolic studies was undertaken.

The first series of experiments was made on five apparently normal male infants between the ages of 11 days and 6 months. They were fed alternately with breast milk and modified cow's milk, six days on each diet, and analysis was made of the calcium, magnesium, phosphorus, and chlorid content of both urine and feces. On the first three days of each period no specimens were collected, thus giving an opportunity for the child to become adjusted to the change from one milk to the other. In changing from breast milk to cow's milk, feedings of cow's milk were substituted for breast feedings gradually, instead of making the complete transition at one time. The same procedure was followed in changing from cow's milk to breast milk. This prevented the onset of gastro-intestinal disturbances. Twenty-four-hour specimens of urine and feces were collected for three days after the diet was established.

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* Received for publication, Jan. 23, 1924.

* From the Nelson Morris Memorial Institute for Medical Research, and the Sarah Morris Hospital for Children of the Michael Reese Hospital.

* This investigation was supported, in part, by the Otto Baer Fund for Clinical Research and by a fund for the study of undernutrition in children, contributed jointly by the Elizabeth McCormick Memorial Foundation, Mrs. Francis Neilson, and Mrs. M. L. Rothschild.

The supply of milk for the days when specimens were taken was prepared at the beginning of the experiment. The required amount of breast milk was expressed from three wet-nurses and thoroughly mixed. When the milk was mixed and ready for use, a sample was removed for analysis, while the rest was preserved with formaldehyd in the proportion of 1:40,000. This was not sufficient preservative to cause any change in the taste of the milk or disturbance in digestion. The cow's milk used was pasteurized and modified by the addition of water and dextrimaltose. The mixture was made to approximate the composition of the breast milk for the same infant. This was likewise preserved with formaldehyd. The modification varied with the age and weight of the child, and was designed to assure a normal gain in weight.

Male infants were used exclusively because of the greater facility of collecting specimens. The child was placed on a hammock swung in a bassinet, and kept there for the duration of the experiment. None of the infants showed any signs of discomfort from their position in the hammock. They were weighed before they were placed on the frame and at the end of the time spent there. Urine was collected by means of a Schloss tube, and feces were collected in a pail placed under an opening in the canvas.

No results are reported where there was any loss in food intake either by refusal of the child to take the food or inability to retain it.

Twenty-four-hour specimens of urine were collected, measured, and then preserved with toluol. The feces were collected in an enamel pail and dried in the same pail over a steam bath. The weight was determined by difference, and the dry feces were scraped from the pail, ground, and further dried by placing over sulphuric acid in a vacuum desiccator. They were then preserved in an air-tight glass container. Methods of analysis and experimental data will appear in subsequent papers.

An attempt was made to determine the corresponding mineral content of the blood. For this purpose about 10 c.c. of blood was drawn from the superior longitudinal sinus, centrifuged immediately, and the salts were determined on the plasma. Difficulty was encountered in most cases, however. The reliable results obtained will be discussed in subsequent papers.

EXPERIMENTAL DATA

EXPERIMENT 1.—W. O., one of twin brothers, was a normal baby, 8 weeks and 6 days old, weighing 4.09 kg., when first placed on the metabolism frame. He was tested for four periods each lasting three days, alternating cow's and breast milk, but the first period was discarded because of the loss of a part of a specimen. One week was allowed for the change of diet between each two periods. He was apparently normal during the whole experiment, which covered a period of thirty-two days; during this time he gained 360 gm. The modification of cow's milk during the third period consisted of whole milk, one half; boiled water, one-half, and 3.5 per cent. dextrimaltose.

Experiment 2.—E. M. admitted to hospital at the age of 5 months for the metabolic experiment, was normal in every respect, and weighed 7.34 kg. at this time. His first period on the frame was with whole milk, two-thirds; boiled water, one-third, and 3 per cent. dextrimaltose, receiving five 7 ounce (207 c.c.) feedings daily. During these three days he gained 120 gm. but during the period of change of diet he lost 150 gm. The second period, five days after the end of the first period, consisted of only two days on breast milk, during which time he gained 30 gm. However, he seemed to be in good health.

Experiment 3.—T. O., twin brother of W. O., was also a normal baby, smaller than his twin. He was 12 weeks and 6 days old, weighing 3.54 kg., when first put on the frame on a diet of breast milk, receiving six feedings of 4 ounces (118.4 c.c.) each. During this period he gained 60 gm. A month later he was on the frame again, receiving six 5 ounce (148 c.c.) feedings a day of a mixture of 17 ounces (503 c.c.) of whole milk, 12 ounces (355 c.c.) of boiled water, and 1 ounce (28.3 gm.) of dextrimaltose. During this period he lost 60 gm., otherwise he was quite well.

Experiment 4.—B. N., born in the hospital, was also normal. He was first put on the frame when 11 days old, weighing 3.24 kg., with seven 3 ounce (89 c.c.) feedings consisting of whole milk, one-half; boiled water, one-half, and 4 per cent. dextrimaltose. He gained 60 gm. during the three days. When a month old he was on the frame again with seven 3½ ounce (104 c.c.) feedings of breast milk each day. In this period he gained 112 gm. He was in good health throughout the experiment.

Experiment 5.—B. B., admitted to the hospital when four hours old because his mother was unable to take care of him, was a normal baby. He was observed for six periods, lasting three days each, three on cow's milk and three on breast milk. He gained in each breast milk period. In the first period on cow's milk at 5 weeks of age he neither gained nor lost. His greatest gain was at the age of 9 weeks on a diet of cow's milk. At this time he gained 142 gm. He was first put on the frame at the age of 5 weeks, weighing 3.82 kg., on a mixture of whole milk, one-half; boiled water, one-half, and 4 per cent. dextrimaltose, seven 4 ounce (118.4 c.c.) feedings. During the second period on cow's milk he received seven 4½ ounce (133.4 c.c.) feedings of a mixture of 18 ounces (532 c.c.) whole milk, 14 ounces (414 c.c.) boiled water, and 1 ounce (28.3 gm.) dextrimaltose. His third period on cow's milk came at the age of 27 weeks. He then received five 7½ ounce (222 c.c.) feedings of a mixture of whole milk, two-thirds; boiled water, one-third, and 4 per cent. dextrimaltose. His first period on breast milk was at the age of 6½ weeks, when he received seven 4 ounce (118.4 c.c.) feedings daily; during the second, at 11 weeks, he had seven 4½ ounce (133.4 c.c.) feedings; and during the third, at 4⅙ months, he had six 6 ounce (178 c.c.) feedings daily. He was a well nourished child and in good health during all the experimental periods.

CALCIUM METABOLISM[1]

The work reported in this paper was designed to compare the utilization of the calcium of breast milk with that of cow's milk by the same infant. Since little other work has been done on this particular problem, opportunity is lacking for comparison of our work with that of other investigators. In the course of our experiments, however, so many points have come up on the general problem of calcium metabolism, where our findings vary considerably from those previously reported, that we have deemed it advisable to discuss the general question of calcium metabolism in infants fed on breast milk and cow's milk, as well as the calcium metabolism in the same infant fed on both breast and cow's milk.

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[1] Metabolism Studies Reported by Chi Che Wang, Ph.D., and Augusta R. Felcher, A. B.

REVIEW OF LITERATURE

Much work has been done on the subject of calcium metabolism, but the comparison was almost invariably made on different infants. The only literature that we were able to find on the calcium metabolism of the two kinds of milk by the same infant is the paper reported by Peiser.[2] His study was made on four infants, only two of whom were normal. His figures for the calcium utilization and calcium retention with both kinds of milk are rather low. His results, along with ours, are shown below.

Blauberg[3] and Hoobler[4] found a higher utilization of calcium from breast milk than from cow's milk. Their conclusions represent a comparison of different subjects. The latter author notes, however, that the calcium intake in cow's milk is about eight times as great as in breast milk, and that the actual amount retained and absorbed is about four times as great. He concludes that the calcium of breast milk is much better metabolized than that of cow's milk, and since a healthy nursing infant shows no deficiency of calcium, the amount that it receives is evidently the true measure of the calcium required. Calcium is eliminated almost entirely through the feces; only from 5 to 10 per cent. of the intake appearing in the urine. There is little variation in the amount of calcium eliminated in the urine of infants fed on breast and cow's milk; in the feces there is great variation. In the case of cow's milk feeding, calcium makes up from one-quarter to one-third of the dried feces. This author finds great individual difference in the amount of calcium absorbed, and a further difference in the ability to retain the calcium absorbed. Givens,[5] on the other hand, states that an increased

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2. Peiser, A.: Beiträge zur Kenntnis des Stoffwechsels, besonders der Mineralien im Säuglingsalter, IV. Vergleichende Untersuchungen über den Stoffumsatz bei Ammenmilch und Eiweissmilch mit besonder Berücksichtizung des Schwefelhaushaltes, Jahrb. f. Kinderh. **81**:437, 1915.

3. Blauberg, M.: Experimentelle Beiträge zur Frage über den Mineralstoffwechsel beim künstlich enrährten Säugling, Ztschr. f. Biol. **40**:1, 1900; Ueber den Mineralstoffwechsel beim natürlich ernährten Säugling, Ztschr. f. Biol. **40**:36, 1900.

4. Hoobler, B. R.: The Rôle of Mineral Salts in the Metabolism of Infants. Am. J. Dis. Child. **2**:106 (Aug.) 1912.

5. Givens, M. H.: Calcium and Magnesium Metabolism in Man, J. Biol. Chem. **34**:119 (April) 1918.

intake of calcium in the form of milk gives rise to an increased urinary output of calcium. Calcium absorption bears no relation to the body weight, but is influenced by the diet and by the tissue reserves of the subject.

Hamilton[6] and Telfer,[7] like Hoobler, find that calcium is excreted mainly in the feces, the amount depending largely on the percentage of calcium in the diet. Hamilton worked with premature, breast-fed infants, and found that three-fourths of them had a low calcium retention during the first months of life; this may have been due to rachitis, as craniotabes appeared in the second month. Where the intake exceeded 0.200 gm. the calcium retention was sufficient, a lower intake resulted usually in insufficient retention. Telfer used cow's milk for his subjects, and noted that when the calcium intake was low diarrhea often ensued. When an excess of calcium was present in the diet, there was increased excretion in the feces and a slight rise in the urinary calcium, the latter denoting an increase in calcium absorption.

Rothberg[8] reports that calcium retention varies little, between from 14 to 26 per cent. of the calcium intake. In general, a large intake is followed by a large retention, and vice versa, but there is no definite relation. Wolff[9] noted that an increase in calcium intake caused an immediate change of the calcium balance from negative to positive.

Orgler,[10] in a monograph published in 1912, on the calcium metabolism of infants, included a comprehensive table of the work then published on this subject, and concluded therefrom that 0.130 gm. of calcium monoxid daily is the minimum of normal retention. Hamilton,[11] in his later work on premature infants, found only five out of twelve whose calcium retention attained this magnitude. He found also a certain correlation between calcium retention and the age and weight of the child. In infants under 3 months the retention is from 0.042 to 0.093 gm. daily, and in infants over 3 months it is from 0.127 to 0.181 gm. daily. There is wide individual variation, however.

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[6] Hamilton, B.: The Calcium Metabolism of Premature Infants, Am. J. Dis. Child. **20**:316 (Oct.) 1920.

[7] Telfer, S. V.: The Influence of Free Fatty Acids in the Intestinal Contents on the Excretion of Calcium and Phosphorus, Biochem. J. **15**:347, 1921; Studies on Calcium and Phosphorus Metabolism. The Excretion of Calcium and Phosphorus, Quart. J. Med. **16**:45 (Oct.) 1922.

[8] Rothberg, O.: Ueber den Einfluss der organischen Nahrungskomponenten (Eiweiss, Fett, Kohlehydrate) auf den Kalkumsatz künstlich genährter Säuglinge, Jahrb. f. Kinderh. **66**:69, 1907.

[9] Wolff, G.: Ueber den Kalk-und Phosphorsäurestoffwechsel des Säuglings bei knapper und reichlicher Ernährung mit Kuhmilch, Jahrb. f. Kinderh. **76**:180, 1912.

[10] Orgler, A.: Ueber den Kalkstoffwechsel bei Rachitis, Monatschr. f. Kinderh. **10**:373, 1911.

[11] Hamilton, B.: The Calcium and Phosphorus Metabolism of Prematurely Born Infants, Acta Pediat. **2**:1, 1922.

METHOD

The excretions were prepared as described above. About 2½ gm. of the finely powdered feces was accurately weighed into a silica crucible, 2 c.c. of concentrated sulphuric acid was added, and the whole was put in the oven to ash. The ash was dissolved in 50 c.c. of 10 per cent. hydrochloric acid, made up to 100 c.c. with distilled water, and filtered through a dry, ashless filter. The calcium determinations were then made according to McCrudden's [12] method. For the calcium determination in urine and milk, also, McCrudden's method was carefully followed. Two hundred cubic centimeters of urine was used for each determination. In the determination of milk, about 10 gm. was accurately weighed into a silica crucible, 1 c.c. of concentrated sulphuric acid was added, and the mixture allowed to ash. The ash was dissolved in 25 c.c. of 10 per cent. hydrochloric acid, made up to 100 c.c. with distilled water and filtered in the same way as the feces. From that point on, the same author's method as for feces was used. In the urine the gravimetric method was employed, but for the calcium determination in feces and in milk the calcium was titrated with potassium permanganate.

All determinations were made in duplicate, and the results given below are the average of the two.

Since Holt [13] and Holt and Fales [14] reported a relationship between calcium metabolism and fat intake, the fat in the milk was determined by the Babcock method in these experiments. These authors report that calcium absorption is aided by a relatively high fat content, giving as the minimum fat requirement from 3 to 4 gm. per kilogram. They also state that a desirable amount of calcium in the diet is represented by the ratio of from 0.03 to 0.05 gm. of calcium monoxid to 1 gm. of fat. Our fat intake per kilogram was never below the minimum figure here given, whereas the ratio of fat to calcium monoxid was slightly lower in breast milk and somewhat higher in cow's milk. However, the slight variation in this ratio did not seem to have any effect on the calcium metabolism; in fact, the case of highest calcium utilization and retention, which occurred with breast milk, showed a fat calcium monoxid ratio of slightly less than 1 : 0.003, and the case where the ratio was high,

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[12] McCrudden, F. H.: The Quantitative Separation of Calcium and Magnesium in the Presence of Phosphates and Small Amounts of Iron Devised Especially for the Analysis of Foods, Urine, and Feces, J. Biol. Chem. **7**:83, 1911; The Determination of Calcium in the Presence of Magnesium and Phosphates; the Determination of Calcium in Urine, J. Biol. Chem. **10**:187, 1911.

[13] Holt, L. E.; Courtney, A. M., and Fales, H. L.: Calcium Metabolism in Infants and Young Children and Relation of Calcium to Fat Excretion in Stools, Am. J. Dis. Child. **19**:97 (Feb.), 201 (March) 1920.

[14] Holt, L. E., and Fales, H. L.: Calcium Absorption in Children on a Diet Low in Fat, Am. J. Dis. Child. **25**:247 (March) 1923.

1 : 0.09, showed a percentage calcium utilization and retention of 52.0 and 51.5 respectively, which are next to the maximum figures for cow's milk.

CONCLUSIONS

Table 1 shows that with the exception of one period in Case 1, the daily value of calcium excretion in the feces varies greatly. The maximum variation occurs in the case of E. M. where, of two successive days, 0.4513 gm. of calcium monoxid was excreted on the first day; this was 2.6 times as great as the amount on the second day, which showed 0.1730 gm. The nonconcordant results may be owing chiefly to the failure always to empty the bowels completely at the end of every twenty-four hours. It is clear, then, that for metabolic investigations the study of individual twenty-four-hour specimens, or one single twenty-four-hour specimen, has little or no value. However, as Table 2 shows, the average daily output of three-day periods gives results which bear distinct differences brought about by a change of diet. Although our analyses were made on twenty-four-hour specimens, our discussion will be based on the average of three consecutive day periods.

With the urine the daily variation is not so marked. Since the amount of calcium in urine is so small—only a few milligrams in a twenty-four-hour specimen—the difference that does exist may be in part attributed to experimental error.

Difference in the Quantity of Calcium Excretion in Feces and Urine Brought About by the Change of Milk.—Table 2, which gives the average daily value per three-day period, shows that a change of milk brought about a distinct change in the quantity of calcium excreted in the feces in every child. The quantity of calcium excreted is invariably greater when the infant is on a diet of cow's milk. The difference of calcium as calcium monoxid in the excretions of the same child ranged from 0.0726 to 0.7829 gm. with an average of 0.4639, which is in agreement with that reported by Peiser,[2] who in his investigation tried two five-day periods on two normal patients. One period on each child was tested with breast milk and the other with cow's. Tables 3 and 4 show that in both cases the change from breast milk to cow's milk brought a large increase in the excretion of calcium in the feces. With breast milk the calcium in the feces in one case was 0.287 and in the other 0.211 gm. When the diet was changed to cow's milk, the calcium monoxid excreted was 0.894 gm. in the first case and 0.591 gm. in the second, which gives an increase of 0.607 and 0.380 gm. respectively, with an average of 0.493 gm.

In the case of the last of our periods tried on B. B. (Table 2), the first and last were with cow's milk and the second and third with breast milk. We see that the quantity of calcium monoxid excreted in the

TABLE 1.—*Daily Calcium Metabolism in Healthy Infants Fed on Breast Milk and Cow's Milk*

Name	Kind of Milk	Date	CaO Intake		CaO Output				CaO Utilization			CaO Retention		
			Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Feces per 24 Hours, Gm.	Urine per 24 Hours, Gm.	Total per 24 Hours, Gm.	Total per Kg. per 24 Hours, Gm.	Per 24 Hours, Gm	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake
W. O	Breast.....	11/26/21	0.6452	0.157	0.2678	0.0171	0.2849	0.069	0.3774	0.092	58.5	0.3603	0.088	55.8
		11/27/21	0.6452	0.156	0.2680	0.0074	0.2754	0.066	0.3772	0.091	58.5	0.3698	0.090	57.3
		11/28/21	0.6452	0.155	0.2687	0.0178	0.2865	0.069	0.3765	0.090	59.2	0.3587	0.086	55.6
	Cow's......	12/ 7/21	1.0932	0.250	0.7357	0.0109	0.7484	0.171	0.3575	0.081	32.5	0.3448	0.079	31.5
		12/ 8/21	1.0932	0.248	0.5041	0.0112	0.5153	0.117	0.5891	0.134	53.9	0.5779	0.131	52.9
		12/ 9/21	1.0932	0.249	0.6356	0.0213	0.6569	0.149	0.4576	0.104	41.9	0.4363	0.100	39.9
	Breast.....	12/16/21	0.6285	0.140	0.2796	0.0174	0.2970	0.067	0.3489	0.078	55.5	0.3315	0.073	52.7
		12/17/21	0.6285	0.141	0.1952	0.0181	0.2133	0.047	0.4333	0.097	68.9	0.4152	0.094	66.0
		12/18/21	0.6285	0.141	0.2445	0.0106	0.2551	0.057	0.3840	0.086	61.1	0.3734	0.084	59.4
E. M	Cow's......	11/26/21	1.5700	0.212	1.0400	0.0083	1.0483	0.142	0.0530	0.071	33.8	0.5217	0.070	33.2
		11/27/21	2.6160	0.351	1.4510	0.0162	1.4672	0.196	0.1165	0.156	44.6	1.1488	0.155	43.9
		11/28/21	2.6550	0.356	0.7941	0.0105	0.8046	0.108	0.1861	0.249	70.1	1.8504	0.248	69.7
	Breast.....	12/ 3/21	0.8861	0.121	0.4513	0.0129	0.4642	0.063	0.4348	0.059	49.1	0.4219	0.058	47.6
		12/ 4/21	0.8982	0.122	0.1730	0.0141	0.1872	0.025	0.7252	0.098	80.7	0.7111	0.097	79.1
T. O.	Breast.....	12/13/21	0.5235	0.148	0.0930	0.0093	0.1023	0.028	0.4305	0.121	82.2	0.4212	0.119	80.5
		12/14/21	0.5235	0.148	0.0930	0.0093	0.1023	0.028	0.4305	0.121	82.2	0.4212	0.119	80.5
		12/15/21	0.5235	0.145	0.0902	0.0252	0.1154	0.032	0.4333	0.120	83.6	0.4081	0.113	77.9
	Cow's......	1/14/22	1.4630	0.360	0.6745	0.0194	0.6859	0.169	0.7885	0.194	53.9	0.7721	0.191	53.1
		1/15/22	1.4630	0.360	0.6745	0.0194	0.6859	0.169	0.7885	0.194	53.9	0.7721	0.191	53.1
		1/16/22	1.4630	0.367	0.7308	0.0150	0.7458	0.186	0.7322	0.183	50.1	0.7172	0.181	49.0
B. N.	Cow's......	3/ 9/22	0.6704	0.269	0.5105	0.0172	0.5277	0.163	0.1599	0.049	23.9	0.1427	0.106	21.3
		3/10/22	0.6704	0.269	0.5157	0.0222	0.5379	0.166	0.1547	0.048	23.1	0.1305	0.103	19.4
		3/11/22	0.6704	0.263	0.2219	0.0183	0.2402	0.073	0.4485	0.136	66.9	0.4302	0.190	64.1
	Breast.....	3/30/22	0.7821	0.217	0.3049	0.0055	0.3104	0.086	0.4772	0.132	61.0	0.4717	0.131	60.3
		3/31/22	0.7821	0.217	0.3049	0.0055	0.3104	0.086	0.4772	0.132	61.0	0.4717	0.131	60.3
		4/ 1/22	0.7821	0.217	0.4204	0.0131	0.4335	0.120	0.3617	0.099	46.3	0.3486	0.097	44.5
B. B.	Cow's......	2/25/22	1.0230	0.267	0.6840	0.0178	0.7017	0.184	0.3390	0.089	33.1	0.3213	0.083	31.4
		2/26/22	1.0230	0.267	0.6840	0.0178	0.7017	0.184	0.3390	0.089	33.1	0.3213	0.083	31.4
		2/27/22	1.0230	0.267	0.6241	0.0175	0.6416	0.160	0.3989	0.104	39.0	0.3814	0.107	37.2
	Breast.....	3/ 8/22	0.7196	0.180	0.1867	0.0141	0.2008	0.050	0.5329	0.133	74.0	0.5188	0.130	72.0
		3/ 9/22	0.7196	0.180	0.3056	0.0164	0.3220	0.081	0.4140	0.104	57.5	0.3976	0.099	55.2
		3/10/22	0.7196	0.180	0.3111	0.0160	0.3271	0.082	0.4085	0.102	56.8	0.3925	0.098	54.6
	Cow's......	3/29/22	1.4680	0.330	0.5857	0.0158	0.6015	0.135	0.8823	0.198	60.1	0.8665	0.195	59.0
		3/30/22	1.4680	0.330	0.8690	0.0186	0.8876	0.199	0.5990	0.135	40.8	0.5804	0.131	39.5
		3/31/22	1.4680	0.330	0.8690	0.0186	0.8876	0.199	0.5990	0.135	40.8	0.5804	0.131	39.5
	Breast.....	4/11/22	0.6446	0.138	0.3035	0.0168	0.3203	0.069	0.3411	0.073	52.9	0.3243	0.069	50.3
		4/12/22	0.7147	0.153	0.3824	0.0137	0.3961	0.086	0.5323	0.071	46.5	0.3186	0.067	44.5
		4/13/22	0.7147	0.153	0.2370	0.0105	0.2475	0.054	0.4777	0.102	66.8	0.4672	0.099	65.3
	Breast.....	5/23/22	0.7608	0.138	0.3387	0.0147	0.3534	0.064	0.4221	0.076	55.5	0.4074	0.074	53.5
		5/24/22	0.8851	0.155	0.2008	0.0248	0.2256	0.040	0.6543	0.119	76.5	0.6295	0.115	73.6
		5/25/22	0.8024	0.146	0.3924	0.0199	0.4123	0.075	0.4100	0.074	51.1	0.3901	0.071	48.6
	Cow's......	7/10/22	1.9030	0.279	0.4835	0.0287	0.5122	0.075	1.4195	0.209	74.6	1.3908	0.204	73.0
		7/11/22	1.9030	0.279	0.5674	0.0267	0.5941	0.087	1.3356	0.206	70.2	1.3089	0.192	68.7
		7/12/22	1.9030	0.279	0.9504	0.0222	0.9726	0.142	0.9526	0.140	50.1	0.9304	0.137	48.8

TABLE 2.—*Average Daily Calcium Metabolism of Healthy Infants Fed on Breast Milk and Cow's Milk*

Name	Age in Mos.	Body Weight, Kg.	Kind of Milk	Fat in Milk, per Cent.	CaO Intake		CaO Output				CaO Utilization			CaO Retention		
					Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Feces per 24 Hrs., Gm.	Urine per 24 Hrs., Gm.	Total per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake
W. O.	2.6	4.13	Breast	4.0	0.6452	0.156	0.2682	0.0141	0.2822	0.068	0.3770	0.091	58.4	0.3630	0.088	56.2
	3.0	4.39	Cow's	...	1.0932	0.248	0.6257	0.0144	0.6401	0.146	0.4681	0.106	42.8	0.4530	0.102	41.4
	3.3	4.46	Breast	4.4	0.6285	0.141	0.2397	0.0154	0.2551	0.057	0.3887	0.087	61.9	0.3734	0.084	59.4
E. M.	5.5	7.43	Cow's	2.2	2.2800	0.307	1.0950	0.0116	1.1066	0.149	1.1850	0.161	52.0	1.1736	0.159	51.5
	5.7	7.33	Breast	3.8	0.8921	0.121	0.3121	0.0130	0.3251	0.044	0.5800	0.079	65.0	0.5665	0.077	63.6
T. O.	3.2	3.57	Breast	4.0	0.5235	0.147	0.0921	0.0146	0.1067	0.029	0.4314	0.121	82.4	0.4168	0.117	79.6
	4.3	4.03	Cow's	2.2	1.4630	0.363	0.6932	0.0179	0.7059	0.174	0.7697	0.190	52.6	0.7538	0.188	51.7
B. N.	0.4	3.26	Cow's	2.1	0.6704	0.206	0.4160	0.0193	0.4353	0.133	0.2545	0.078	37.9	0.2344	0.073	35.1
	1.4	3.61	Breast	3.6	0.7821	0.217	0.3434	0.0080	0.3514	0.097	0.4387	0.121	56.9	0.4323	0.119	55.1
B. B.	1.3	3.82	Cow's	2.0	1.0230	0.267	0.6640	0.0177	0.6816	0.178	0.3590	0.094	35.1	0.5120	0.089	33.4
	1.6	3.99	Breast	4.2	0.7196	0.180	0.2678	0.0155	0.2833	0.071	0.4518	0.113	62.8	0.4363	0.109	60.6
	2.1	4.44	Cow's	2.2	1.4680	0.330	0.7746	0.0177	0.7922	0.178	0.6934	0.156	47.2	0.6758	0.152	46.0
	2.4	4.66	Breast	3.3	0.6913	0.148	0.3076	0.0137	0.3213	0.070	0.3837	0.082	55.5	0.3700	0.078	53.5
	4.6	5.50	Breast	3.3	0.8161	0.146	0.3106	0.0198	0.3304	0.060	0.4954	0.090	61.5	0.4756	0.086	59.0
	6.1	6.82	Cow's	2.0	1.9030	0.279	0.6671	0.0259	0.6930	0.101	1.2359	0.183	65.0	1.8150	0.178	63.5

feces of the two breast milk periods, although six weeks apart, varied only slightly, 0.0030 gm., and was proportional to the age of the child. The amount excreted with cow's milk during the period immediately preceding and the one immediately following the two breast milk periods is more than twice as much as that excreted with breast milk. The difference of calcium excreted between the first and second periods is 0.4670 gm., and that between the third and fourth is 0.3565 gm.

The calcium excretion through the feces in all our cases ranges from 0.0921 gm. to 0.3434 gm., with an average of 0.2677 gm. with breast milk. Fifty per cent. of our cases give higher values than the maximum figures reported by previous investigators. Their values range from 0.0312 to 0.287 (Table 3). With cow's milk our figures ran from 0.4160 gm. to 1.095 gm., with an average of 0.7051 gm., as against their range of 0.5600 to 2.2687. The discrepancy between our results and those of other investigators in the case of breast milk is probably because of the difference in the amount of calcium intake. Our intake per kilogram varied between 0.141 gm. and 0.217 gm., whereas other investigators report a per kilogram intake of 0.047 gm. to 0.088 gm. Hamilton [11] suggests that a rough average calcium intake should be 0.200 to 0.400 gm. daily. Our calcium intake is lower than this, but even so, it is from two to four times higher than that reported in previous work. It is therefore possible that the infants in the experiments reported by previous investigators were not getting sufficient food, at least during the experimental periods, and the amount excreted might thus be the minimum calcium output of each subject. The investigation of this point is now in progress.

On the other hand, our figures for the calcium output in the feces with cow's milk are lower than theirs. This may possibly be owing to the difference in methods of modification. Peiser,[2] for instance, used evaporated milk, and Blauberg [3] used sterilized milk. In all cases where formulas are given, the same formula is used for children of different ages. In our experiments, pasteurized milk was used which was modified with water and dextrimaltose to approximate the individual child's breast milk requirements. Individual formulas are given above. So far as the calcium intake is concerned, our figures run between 0.6704 and 2.280 gm. with an average of 1.4144 gm. as compared with the above mentioned authors, whose intake is from 0.654 to 2.0536 gm.

The difference brought about in the calcium excretion in the urine with a change in diet is slight and inconsistent. Out of nine changes, four were from breast to cow's milk, and five from cow's to breast milk. In the change from breast to cow's milk, the maximum difference was an increase of 6 mg. with cow's milk; in the change from cow's to breast milk, in three cases there was a decrease in the calcium excretion

Table 3.—*Calcium Metabolism of Healthy Infants Fed on Breast Milk*

Author	Subject	Duration of Period, Days	Age in Mos.	Body Weight, Kg.	CaO Intake		CaO Output			CaO Utilization			CaO Retention		
					Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Feces per 24 Hrs., Gm.	Urine per 24 Hrs., Gm.	Total per 24 Hrs., Gm.	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake
Peiser [2]	1	5	3.0	3.800	0.3350	0.088	0.2870	0.0360	0.3230	0.0480	0.0130	14.30	0.0120	0.0030	3.58
	2	...	1.5	3.720	0.2790	0.075	0.2110	0.0210	0.2320	0.0680	0.0180	24.40	0.0480	0.0130	17.07
Tobler-Noll: Monatschr. f Kinderh. **9**: 210, 1910	...	6	2.5	4.040	0.2390	0.059	0.1485	0.0372	0.1857	0.0905	0.0220	37.80	0.0530	0.0133	22.30
Lindberg [18]	1	..	2.5	4.285	0.2572	0.060	0.1827	0.0183	0.2010	0.0745	0.0173	28.90	0.0562	0.0130	21.85
	1	...	...	4.370	0.2615	0.051	0.1748	0.0228	0.1976	0.0867	0.0198	33.10	0.0639	0.0150	24.44
	1	...	...	4.370	0.2397	0.055	0.1895	0.0131	0.2026	0.0502	0.0115	29.40	0.0371	0.0090	11.30
	1	...	...	4.370	0.2089	0.048	0.2201	0.0220	0.2421	−0.0112	−0.0025	.....	−0.0332	−0.0080	.....
Blauberg [3]	...	3	5.0	.....	0.2720	.....	0.0660	0.0310	0.0970	0.2060	......	75.80	0.1750	......	60.62
Michel-Perrett [15]	...	3	3.0	4.725	0.3770	0.080	0.1980	0.0300	0.2280	0.1790	0.0370	47.49	0.1490	0.0320	39.52
Michel [19]	...	3	0.17	3.730	0.2520	0.068	0.0312	0.0124	0.0436	0.2208	0.0590	87.50	0.2090	0.0560	82.80
		4	0.17	2.680	0.2317	0.086	0.0951	0.0076	0.1027	0.1367	0.0510	58.70	0.1290	0.0480	55.60
		6	0.23	3.500	0.2965	0.085	0.0950	0.0076	0.1026	0.2015	0.0570	68.00	0.1940	0.0550	65.50
		3	0.37	4.400	0.3010	0.068	0.0860	0.0147	0.1007	0.2150	0.0490	71.30	0.2000	0.0460	66.70
Schabad [16]	..	3	3.75	7.685	0.3636	0.047	0.1640	0.0186	0.1826	0.1996	0.0530	54.89	0.1810	0.0490	49.79

TABLE 4.—*Calcium Metabolism of Healthy Infants Fed on Cow's Milk (Modified)*

Author	Subject	Duration of Period, Days	Age in Mos.	Body Weight, Kg.	CaO Intake		CaO Output			CaO Utilization			CaO Retention		
					Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Feces per 24 Hrs., Gm.	Urine per 24 Hrs., Gm.	Total per 24 Hrs., Gm.	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per Cent. of Intake
Peiser [2]	1	5	3.0	3.80	0.8740	0.230	0.8940	0.0500	0.9440	—0.0150	—0.004	.....	—0.0700	—0.019	.....
	2	5	1.5	3.70	0.7280	0.197	0.5910	0.0570	0.6480	0.1370	0.037	18.80	0.0800	0.022	11.01
Blauberg [3]	...	4	..	....	0.7520	.....	0.5840	0.0140	0.5980	0.1680	.....	22.36	0.1540	.....	20.48
Telfer [7]	1	8	15.0	8.30	0.8200	0.099	0.6700	.. ...	... ..	0.1500	0.018	18.30	......	.....	.....
	2	...	8.0	6.50	0.8200	0.126	0.6800	0.0020	0.6820	0.1400	0.021	17.07	0.1380	0.021	16.08
	3	...	9.0	9.40	0.8000	0.085	0.5600	......	......	0.2400	0.025	30.00	......	.....	.....
	1	...	6.0	6.45	0.8100	0.126	1.0000	0.0160	0.0160	—0.1900	—0.029	.....	—0.2060	—0.032	.....
Cronheim and Müller [17]	1	3	4.5	4.95	0.6540	0.132	0.8420	0.0150	0.8570	—0.1880	—0.038	.....	—0.2030	—0.041	.....
	2	4	6.0	6.50	1.2750	0.196	1.1910	0.0118	1.2028	0.0840	0.013	6.58	0.0722	0.011	5.74
	3	4	4.0	6.90	1.3530	0.196	0.9180	0.0170	0.9350	0.4350	0.063	32.13	0.4180	0.060	30.87
	4	4	4.0	3.84	0.8660	0.226	0.6820	0.0108	0.6928	0.1840	0.048	21.28	0.1732	0.045	20.03
	5	4	6.0	7.80	1.4130	0.181	1.3520	0.0438	1.3958	0.0610	0.008	4.30	0.0170	0.002	1.20
Hoobler [4]	...	...	...	....	2.0536	.....	2.2687	0.0301	2.2988	—0.2151	.....	.....	—0.2452	.....	.....

with breast milk and in two there was an increase; the maximum increase was 2 mg. and the maximum decrease was 11 mg. With breast milk the calcium excretion through the urine in all the children runs between 0.008 gm. and 0.0198 gm., with an average of 0.0143 gm.; while with cow's milk it lies between 0.0116 gm. and 0.0259 gm., with an average of 0.0178 gm. We see, therefore, that with cow's milk there is a slight increase in the average value. In the two cases reported by Peiser [2] the calcium excretion in urine with breast milk was 0.036 gm. in the first case and 0.021 gm. in the second; with cow's milk it was 0.050 and 0.057 gm., respectively. His difference is therefore 0.014 gm. in the first child and 0.036 gm. in the second, with an average of 0.025 gm. This is more than twice as high as the maximum difference in our infants. The calcium excretion through the urine in all the cases reported in Table 3 lies between 0.008 and 0.037 gm. with breast milk, and from 0.002 to 0.057 gm. with cow's milk. Because of the very small amounts of calcium involved in the urinary excretion and the possibility of experimental error, it is difficult to say whether there is any significance in the different results.

The Effect of the Change of Milk on the Utilization and Retention of Calcium.—This is well marked. Aside from B.N., the actual quantity of calcium utilized is greater with cow's than with breast milk. With the former the calcium utilization per twenty-four hours runs from 0.2545 to 1.2359 gm., with an average of 0.7094 gm., while with the latter it varies between 0.3770 and 0.5800 gm., with an average of 0.4433 gm. With breast milk the calcium utilization per twenty-four hours reported by previous investigators and summarized in Tables 3 and 4 lies between —0.0112 and +0.2208 gm., and with cow's milk it is from — 0.1880 to + 0.4350. Of the fourteen periods on breast milk and thirteen periods on cow's milk tried by these authors, one period gave a negative balance with the former and four periods with the latter. In our cases we had no negative balance with either kind of milk. These figures show that the quantity utilized with both cow's and breast milk is much greater in our work than in the work reported by the above authors. Our minimum value is greater than the maximum reported in Table 3 with breast milk, and with the exception of one case the same holds true in Table 4 for cow's milk. In agreement with their figures, however, the actual quantity of calcium utilized is greater with cow's than with breast milk, the average figures being 0.7094 as against 0.4433 gm.

The percentage utilization of calcium is almost invariably greater with breast milk. The only period which showed a greater percentage of utilization with cow's milk is the last period of the work on B.B. This difference is probably due to difference in age, which will be discussed later. The percentage utilization with breast milk is between 55.50 and 82.40 with an average of 63.04; with cow's milk it is from 35.09 to 64.95 with an average of 47.51. With the exception of the figures showing a negative balance, the other investigators report percentages ranging from 11.80 to 87.50 for breast milk. For cow's milk their values are from 4.30 to 32.13. In all cases except those of Blauberg,[3] Michel,[15] and Schabad,[16] the percentage utilization of breast milk is less than our minimum figure. The difference in the case of cow's milk is even greater. The discrepancy may be accounted for by the criticism of Schabad [16] and Hamilton,[6] who have pointed out that the work of Blauberg [3] and Cronheim and Müller [17] may be criticized on the ground of insufficient intake of milk or insufficient calcium content of the milk fed. Hamilton criticizes Schabad on the same point.

Since the amount of calcium excreted in the urine is rather insignificant and fairly constant, the effect of a changed milk diet on the retention of calcium is similar to that on the utilization. The actual amount retained with cow's milk is greater in every case except in that of B.N.

In breast milk the actual amount of calcium retained ranges from 0.3630 to 0.5665 gm. per twenty-four hours, an average of 0.4524 gm., and a per kilogram range of from 0.077 to 0.119 gm. The range with cow's milk is from 0.2344 to 1.815 gm. per twenty-four hours, an average of 0.8025 gm., and a per kilogram range of from 0.073 to 0.188 gm. This is a much greater range for cow's milk in both total and relative amounts of calcium retained. Aside from the negative results of Lindberg,[18] the range for breast milk obtained by other investigators is from 0.003 to 0.2090 gm. per twenty-four hours, with a per kilogram range of 0.0019 to 0.0560 gm. With eleven cases of cow's milk feeding reported by other investigators four cases give a negative calcium balance. The rest range from 0.0170 to 0.4180 gm. retention per twenty-four hours, with a per kilogram range of from 0.002 to 0.060 gm. The figures show clearly that our work is much more uniform, showing a per kilogram variation in range of from one and a half times the minimum value in case of breast milk to two and a half times for cow's milk, as against their variation of more than fifty times for breast milk and thirty times for cow's milk. This holds true not only by comparison with all cases, but also by comparison with the work of individual investigators. For example, Lindberg [18] worked with the same infant fed with breast milk for four periods, and found a variation of —0.008 to 0.015 gm. per kilogram, or three times the minimum value. The variation of the work reported by Cronheim and Müller [17] with cow's milk is far greater. The retention per kilogram ranged from —0.0041 to 0.4180 gm., which is about 103 times the minimum. On the other hand, the work of Michel [19] is more consistent, and he reports a relative range even smaller than ours. His calcium retention per kilogram per twenty-four hours for breast milk is from 0.046 to 0.056 gm., which is less than one and a quarter times the minimum.

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[15] Michel, C.: Recherches, sur la nutrition normale, du nouveau-né echanges nutritifs azotés et salins, L'obstétrique, **1**:140, 1896.

[16] Schabad, J. A.: Zur Bedeutung des Kalkes in der Pathologie der Rachitis, Arch. f. Kinderh. **54**:83, 1910.

[17] Cronheim, W., and Müller, E.: Versuche über den Stoff—und Kraftwechsel des Säuglings mit besonderer Berücksichtung des organisch gebundenen Phosphors, Ztschr. f. diätet. u. physik. Therap. **6**:25, 1903; Untersuchungen über den Einfluss der Sterilisation der Milch auf den Stoffwechsel des Säuglings unter besonderer Berücksichtung der Knochenbildung, Jahrb. f. Kinderh. **57**:45, 1903; Stoffwechselversuche an gesunden und rachitischen Kindern mit besonderer Berücksichting des Mineralstoffwechsels, Biochem. Ztschr. **9**:76, 1908.

[18] Lindberg, G.: Ueber den Stoffwechsel des gesunden, natürlich ernährten Säuglings und dessen Beeinflussung durch Frauenmilchfett, Ztschr. f. Kinderh. **16**:90, 1917.

TABLE 5.—*Relation of Age to Calcium Metabolism, Breast Milk*

Name	Age in Months	CaO Utilization		CaO Retention	
		Gm. per 24 Hours	Per Cent. of Intake	Gm. per 24 Hours	Per Cent. of Intake
B. N.	1.4	0.4387	56.9	0.4323	55.1
B. B.	1.6	0.4518	62.8	0.4363	60.6
B. B.	2.1	0.3837	55.5	0.3700	53.4
W. O.	2.6	0.3770	58.4	0.3630	56.2
T. O.	3.2	0.4314	82.4	0.4168	79.6
W. O.	3.3	0.3887	61.9	0.3734	59.4
B. B.	4.6	0.4954	61.5	0.4756	59.0
E. M.	5.7	0.5800	65.0	0.5665	63.6

The percentage retention of breast milk calcium in our cases is from 53.5 to 79.6; that of Michel runs from 49.79 to 82.80, while the range of all other investigators reported is from 1.11 to 82.80, disregarding negative values. Excluding Michel's results, there was only one case which attained our minimum value. In the case of cow's milk, our range is from 33.4 to 63.5 per cent.; that of other investigators, aside from the four cases of negative balance, is from 1.2 to 30.87 per cent. Thus the percentage retention of calcium in cow's milk is far greater in our work than in any of the experiments previously reported. With such a discrepancy in results it must be concluded that the methods of experimentation used are not comparable. The difference in the modification of cow's milk used has already been mentioned.

Effect of Age on Calcium Metabolism.—An examination of Table 5 shows that the calcium utilization and calcium retention of breast milk are independent of the age of the infant. Thus the percentage utilization in children from 1.4 months to 5.7 months varies within only a

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[19] Michel, C., and Perret, M.: Étude des échanges nutritif azotés et mineraux chez un nourrisson, Bull. Soc. d'obstet. de Paris **2**:98, 1899.

10 per cent. range, with one exceptional case; the percentage retention varies directly with the percentage utilization, also within a 10 per cent. range. It is interesting to note, in the case of B.B., that the utilization and retention are greater at the age of 1.6 months than in either of the later periods. On the other hand, the calcium metabolism of cow's milk (Table 6) shows a distinct increase with the age of the child. Here, in infants from 0.4 to 6.1 months, there is a difference of 27.0 per cent. in utilization and 28.4 per cent. in retention, the higher figures occurring in the older children. Again referring to the case of B.B., we find that here the increase in both utilization and retention is almost proportional to the increase in the age of the child. When this infant was 1.3 months old he showed a calcium utilization of 35.1 per cent. and retention 33.4 per cent.; at 2.4 months the corresponding figures were 47.2 per cent. and 46.0 per cent.; and at 6.1 months, 65.0 per cent. and 63.5 per cent. The percentage utilization of calcium in cow's milk does not reach the average figure of that of breast milk until the child has attained the age of 6 months. Because of the higher calcium content of cow's milk, the actual amount of calcium utilized by the child of 6 months or older is much higher when he is fed on cow's milk than when his diet consists of breast milk. In this connection there is the possibility that a child of 4 months or more does not receive sufficient calcium from a diet of breast milk to secure a maximum gain in weight unless it is supplemented from some other source. For instance, B.B., up to the age of 2.1 months, showed an increase in the calcium metabolism on both breast and cow's milk. This increase continued in the case of cow's milk, but not with breast milk. At the age of 2.1 months his actual utilization and retention of calcium was higher with cow's milk than with breast milk two and a half months later. At 6.1 months the figures for cow's milk are two and a half times the highest figures for breast milk, which occurred at the age of 4.6 months. Hamilton,[11] working with premature infants, also found a correlation between age and calcium metabolism.

TABLE 6.—*Relation of Age to Calcium Metabolism, Cow's Milk*

Name	Age in Months	CaO Utilization		CaO Retention	
		Gm. per 24 Hours	Per Cent. of Intake	Gm. per 24 Hours	Per Cent. of Intake
B. N.	0.4	0.2545	37.9	0.2344	35.1
B. B.	1.3	0.3590	35.1	0.5120	33.4
B. B.	2.4	0.6934	47.2	0.6758	46.0
W. O.	3.0	0.4681	42.8	0.4530	41.4
T. O.	4.3	0.7697	52.6	0.7538	51.7
E. M.	5.5	1.1850	52.0	1.1736	51.5
B. B.	6.1	1.2359	64.9	1.8150	63.5

SUMMARY

1. Owing to the failure completely to evacuate the bowels every twenty-four hours, accurate determinations can be secured only from average values of at least a three day period.

2. A change from breast milk to cow's milk, or vice versa, was invariably accompanied by a change in the quantity of calcium excreted in the feces; the actual quantity excreted was always greater on a diet of cow's milk. The difference in the calcium excretions of the same child ranged from 0.0726 to 0.7829 gm., with an average of 0.4364 gm. The difference in the calcium excretion in the urine brought on by a change in diet is slight and inconsistent.

3. Calcium absorption and retention run closely parallel, since the variation in the urinary calcium output is slight and of little significance.

4. The actual quantity of calcium absorbed and retained is greater for cow's milk than for breast milk, but the percentage utilization and retention is greater for breast milk, except with the older children. With cow's milk, the average utilization is 0.7094 gm. per twenty-four hours, and with breast milk 0.4433 gm. The percentage utilization of cow's milk is 47.5 and of breast milk 63.0. The figures for calcium retention show an average of 0.8025 gm. per twenty-four hours for cow's milk and 0.4524 gm. for breast milk, or a percentage retention in the first case of 46.1 and in the second 60.9.

5. The calcium metabolism of breast milk is independent of the age of the child, but that of cow's milk shows a distinct increase with the age of the child, both in individual cases and in the group of subjects. The percentage utilization and retention of calcium of breast milk in infants from 1.4 months to 5.7 months falls within a range of 10 per cent. In case of cow's milk with children from 0.4 months to 6.1 months, there is a range of 27.0 per cent. in utilization and 28.4 per cent. in retention, the higher figures occurring in case of the older children.

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20. Tobbler, L., and Noll, F.: Zur Kenntnis des Mineralstoffwechsels beim gesunden Brustkind, Monatschr. f. Kinderh. **9**:210, 1910.

ANEMIA IN THE NEW-BORN *

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Anemia of early infancy is of comparatively frequent occurrence, whereas anemia in the new-born is a rare event. The new-born among those babies destined from antenatal causes to become anemic after the lapse of several weeks, or months, almost always manifest at the time of birth and during the early weeks of life the red blood count and hemoglobin of the normal, healthy new-born. This fact is shown by the studies of Lichtenstein [1] on ninety-two premature infants, beginning with their blood findings at birth and continuing for considerable lengths of time. The premature infant at birth presents the high red blood cell count and the high hemoglobin usually found in full term [2] infants, while study of the blood smears shows more pronounced embryonic characters. His anemia appears first after the lapse of weeks or months, eventually becoming the marked and obstinate anemia so familiar in premature infants, which may be moderate or become very severe. In this connection it is of interest to note that of the ten cases of advanced and severe anemia studied by Evans and Happ,[3] six occurred in prematurely born infants, but the anemia described was in babies of several months or more of age. Finkelstein [4] observed that the number of anemic infants among premature babies was generally large from the fourth month on. Beside immaturity of the function of blood formation among these babies, iron has not been sufficiently stored in the liver, a function exercised in full term babies during the last three months of intrauterine life. Premature birth may explain the frequency of anemia in twins, while if they are full term and become anemic, it may be due to the fact that there was not iron [5] enough to go around.

To account for anemia in the early months of life, it is very natural to turn to the mothers of such infants. An explanation may be found in

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* From the Pediatric Department of the George Washington University.

* Received for publication, Jan. 23, 1924.

[1] Lichtenstein, A.: Hematological Studies Upon Premature Infants in Their First Year with Special Reference to Anemia, Svenska läk.-sällsk. handl. **43**:1533-1829 (Dec.) 1917. (Extensive Bibliography.)

[2] Lucas, W. P., et al.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

[3] Evans, F. A., and Happ, W. M.: Secondary Anemia of Infants, Bull. Johns Hopkins Hosp. **33**:1-12 (Jan.) 1922.

[4] Finkelstein, H.: Ueber die Anämien des frühesten Kindesalters, Berl. klin. Wchnschr. **48**:1829-1833, 1911.

[5] Ashby, H. T.: The Relation of Iron to Anemia in Infancy and Childhood, Lancet **2**:150, 1912.

some mothers who have had acute illness while pregnant or who are suffering with tuberculosis or syphilis; in mothers of advanced age and weak constitutions; in neuropathic mothers, particularly with enteroptosis and anemia; and in mothers who have had repeated pregnancies at short intervals with abortions and hemorrhages.

Among other causes of anemia in the early months of life Finkelstein[4] gives the following: (1) a congenital form which is distinguished by absence of swelling of lymph nodes and spleen, with normal blood findings, except reduced hemoglobin and a moderate reduction in the number of red blood cells, and with good reaction to iron therapy; (2) an obstinate infantile anemia due to "plastic weakness in the function of blood formation, of which Virchow and Immerman speak," not readily influenced by iron administration, mixed diet, or other measures, while later the blood forming function gradually increases and the anemia disappears; (3) anemia of hereditary or family predisposition which hangs on in status quo in spite of therapy.

Holt and Howland[6] state that anemia "sometimes occurs in the first two or three months of life in a severe form without any discoverable cause."

Among discoverable causes may be mentioned infection of the young infant with pyogenic organisms, tuberculosis, syphilis, diphtheria, malaria, or other infections. Also traumatic and spontaneous hemorrhages including the hemorrhagic disease of the new-born. It is conceivable that the offspring of a mother addicted to the use during her pregnancy of a hemolytic drug such as acetanilid, might be anemic early in life, also a mother poisoned by mineral poison, benzol or other organic compounds.

Hemolytic jaundice may be manifest soon[7] after birth, and give rise to anemia. That rarer form of familial icterus,[8] sometimes spoken of as icterus gravis, is accompanied by severe, congenital anemia. In both of the latter, however, the icterus is a prominent symptom, while the anemia accompanies it.

The older the infant, the more numerous are the factors that operate to produce an impoverishment of the blood. The von Jaksch type of anemia is most common in the second half of the first year.

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[6] Holt, L. Emmett, and Howland, John: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1922, p. 814.

[7] McKelvey, J. P., and Rosenbloom, J.: Metabolism Study of a Case of Congenital Hemolytic Jaundice with Splenomegaly, Arch. Int. Med. **15**:227-238 (Feb.) 1915.

[8] Buchran, and Comrie: J. Path. & Bacteriol. **13**:398-413, 1909. Rolleston, H.: Ten Postgraduate Lectures, Proc. Roy. Soc. Med., London 31-39, 1922; Practitioner **104**:1-7 (Jan.) 1920. Ylppö: Ztschr. f. Kinderh. **17**:334-362, 1918. Abt, I. A.: Familial Icterus of New-Born Infants, Am. J. Dis. Child. **13**: 231 (March) 1917.

Alimentary anemia[9] also occurs after the period which is being considered.

REPORT OF CASE

History.—F. O., a girl, white, born March 10, 1920, gave a negative family history. The mother, aged 27, had always been in excellent health. She had never used hemolytic drugs. A few weeks after the present baby was born the physical and laboratory examinations were normal (including Wassermann, blood, urine, and stool). The father, aged 33, an officer in the Regular Army, was in good health, and never had syphilis. Blood Wassermann was negative March 22, 1920. A sister of the patient, aged 3½ years, had always been in good health, was breast fed for four months, and was beyond the average child in development. There had been no other pregnancies. So far as known, there had been no contact with tuberculosis.

Labor began ten days prior to the estimated date of confinement, was eleven hours in duration, and without instrumental assistance. The baby weighed 7¾ pounds (3,516 gm.) and was described by the physician who delivered her as of normal, healthy appearance. When she was 11 days old, the nurse stated that she had been unusually pale from birth and that the pallor had been increasing steadily.

She cried well at birth and took the breast readily. March 11, twitchings of the right arm and forehead were noted. March 12, there were twitchings of the right side of the face, right arm and leg, lasting a couple of minutes, followed by the vomiting of "a large quantity of light fluid." Twitchings were observed repeatedly on the second and third days, lasting from one to four minutes. Temperature, the second morning was 101.6, evening, 98.6, and normal thereafter. Minimum weight 7 pounds (3,175 gm.) at 3 days of age. Cyanosis, skin eruptions, and snuffles were absent. Hemorrhages into the skin, from any of the mucous surfaces, and in urine and stools, were lacking.

The appetite was good, the infant having seven nursings in twenty-four hours.

The patient was first seen by me when 11 days old, the chief complaint being pallor of the skin and mucous membranes. The temperature was 97.8, the respirations and pulse being noted as rapid, the weight 7½ pounds (3,402 gm.) the length 20½ inches (51 cm.).

Physical Examination.—The general appearance was that of a strikingly pale baby with good nutrition and development, lying comfortably, breathing quietly but fast, expression calm.

The skin was fair, smooth, of normal turgor, moderately dry, with no signs of icterus, pigmentation, eruption or hemorrhage. The upper eyelids were somewhat puffy, the veins were not visible even on vigorous crying, which caused no reddening of the skin. No desquamation of palms, soles or elsewhere was noted.

The head was well formed and symmetrical. The eyes moved normally; the pupils were equal, medium in size, and contracted to light. The sclera was bluish white. The conjunctiva was very pale. The ears were strikingly pale and bloodless. The drum heads were pearly white, and presented normal landmarks. The nose was well formed, unobstructed, with no excess of secretion. The septum and turbinates were very pale; no signs of hemorrhages. The lips were almost as pale as the white skin, moist, and free of ulcerations. The gums were pale, as were the buccal mucous membranes, tongue and pharynx; the tongue was moist, free of fissures and ulcerations.

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[9] Hutchison, R.: Some Disorders of the Blood and Blood-Forming Organs in Early Life, Goulstonian Lectures, Lancet **1:**1253-1262, 1323-1333, 1402-1409, 1904. Kleinschmidt, H.: Ueber Alimentäre Anämie, Jahrb. f. Kinderh. **83:**221-258, 1916. Lehndorff, H.: Anemia in Children, Monatschr. f. Kinderh. **24:**1-44 (Oct.) 1922. Lucas, W. P., and Hoobler, H. R.: Study of Acute Secondary Anemias in Infancy, Am. J. Dis. Child. **26:**291-302 (Oct.) 1923. Morse, J. L.: Anemias of Infancy, J. A. M. A. **52:**455-463 (Feb. 6) 1909. Opitz, H.: Zur Pathogenese der Anämien im Kindesalter, Klin. Wchnschr. **1:**1769-1773 (Sept. 2) 1922. Poynton, F. J.; Thursfield, H., and Paterson, D.: The Severe Blood Diseases of Childhood, Brit. J. Dis. Child. **19:**57-80 (April-June) 128-143 (July-Sept.) 1922. Schwenke, J.: Ueber Schwere Anämien im frühen Kindesalter, Jahrb. f. Kinderh. **88:**181-203, 284-305, 356-385, 1918.

There was no enlargment of the cervical, axillary, epithrochlear or inguinal lymph nodes, or of the thyroid gland. No cough was present or hoarseness of the cry. The chest was well formed and symmetrical. The respirations were rapid and of the combined abdominal and thoracic types. The lungs were well filled with air and otherwise normal. The heart apex was felt in the fourth space about the nipple line; no enlargement was made out, the sounds were of good quality; a soft, blowing, musical murmur was heard at the base, which was not transmitted. The pulse was very small, weak and rapid. The abdomen was at the same level as the thorax, rounded, soft and mobile.

The liver, which was not enlarged, was felt as a smooth mass below the costal margin. The spleen was barely palpable very slightly below the costal margin. The cord was off the navel, the base of which was very pale, not entirely healed and appeared healthy. The kidneys were not palpable. The joints were freely movable, and the muscles of the limbs and body were of good tone and strong. There were no swellings or tenderness along the bones or the joints. There was nothing abnormal to be seen in the genitalia.

Blood Examination.—March 22, the blood Wassermann was negative, the blood culture, of 1 c.c. of blood showed no growth, red corpuscles, 918,000, hemoglobin, 20 per cent., color index, 1 +, white corpuscles, 29,200, stained smears of polymorphonuclear neutrophils 51.3 per cent., eosinophils 0.7 per cent., basophils 0.0, lymphocytes, 42.0 per cent., large mononuclears and transitionals 2.7 per cent., neutrophil myelocytes, 3.3 per cent.

Fragile white blood corpuscles ("smudges") were fairly numerous. Myelocytes and metamyelocytes, were both present but few in numbers. Several pathologic lymphoid forms were seen.

Nucleated red corpuscles, 10, apparently normoblasts, seen while counting 300 leukocytes; minimal degree of anisocytosis, a few macrocytes; an occasional poikilocyte was seen, extremely rare. The color was essentially normal except for an occasional pale macrocyte. Diffuse basophilia was fairly well marked more common in the cells, larger and paler than normal. Platelets were high normal or moderately increased. No parasites were seen. A probable diagnosis was of secondary anemia. The almost normal color of the red blood corpuscles associated with such a low red count was not to be expected.

March 23, the patient, at 12 days of age, had a transfusion of 100 c.c. of 0.25 per cent. citrated blood given by way of the longitudinal sinus. March 24, the color was greatly improved over that prior to transfusion. Blood examination showed the hemoglobin rose from 20 per cent. before to 45 per cent. after transfusion; the red blood cells rose from 918,000 before to 2,408,000 after transfusion; there were many nucleated red blood cells of both types; 1.5 per cent. of myelocytes; moderate changes in size, shape and staining of red blood cells were as before.

The urine which was of a pale, straw color, contained a trace of albumin, with negative sediment findings.

March 26, the spleen had become enlarged, and was now 1 to 1.5 cm. below the costal margin. The liver was of normal size.

March 27, the hemoglobin had fallen to 35 per cent. and the red blood count to 1,592,000 in four days. Fragmentation of red blood cells was observable (destruction of transfused corpuscles?).

March 28, Fowler's solution of arsenic, one-half drop, three times daily was started.

March 30, the weight was 7½ pounds (3,402 gm.). A second transfusion of 70 c.c. citrated blood was again given with a further notable improvement in color.

Comparison of Two Cases of Anemia in the New-Born

	Author's Case	*Ecklin's Case*
Family history..........	Healthy parents No deaths No miscarriages	Father had heart disease. Mother had grippe and bronchitis when six months pregnant; did not regain her strength. Several infantile deaths, one at 3 days, cause? one of convulsions at 6 months; one miscarriage; the infant born before the patient, died at 17 days of *icterus gravis familiare.*
Birth weight............	7¾ lbs. (3,516 gm.)	2,870 gm. (6 lbs. 5 oz.)
Jaundice	Absent	Present from 1st to 16th days.
Spleen	Very slightly enlarged	Large soft mass 3 cm. below costal border.
Blood Examination at 12 Days of Age:		
Red blood cells.........	918,000	2,500,000
Hemoglobin	20 per cent.	32 per cent.
Color index...........	1.	0.64
White corpuscles.......	29,200	40,000
Red Blood Cells:		
Anisocytosis	slight	marked
Poikilocytosis	rare	frequency, moderate; irregularity, marked
Color	Normal: occasional pale macrocyte	many pale cells
Normoblasts	in moderate numbers	in large numbers
Megaloblasts	few	few
Basophilia:		
diffuse	marked	marked
punctate	slight	"not infrequent"
Reticulated red cells	4.6 per cent. [later]	not stated
White Blood Cells:		
Polymorphonuclears and myelocytes	55.3 per cent.	39.6 per cent.
Lymphocytes	42.0 per cent.	57.8 per cent.
Mononuclears	2.7 per cent.	2.6 per cent.
Total	100.0 per cent.	100.0 per cent.
Metamyelocytes	rare	4.0 per cent.
Myelocytes	3.3 per cent.	numerous
Lymphoid forms (pathologic)	a few	25.0 per cent.
Platelets	increased	not stated
Blood picture normal.....	within 6 months	within 7 months
Spleen, normal size......	at 5 weeks	within 7 months

April 1, at 1 a. m., the temperature was 102.5, at 4 p. m. 101. The spleen was less than 1 cm. below the costal margin.

April 2, the mother and baby left the lying-in-hospital for home. The hemoglobin was 45 per cent.; red blood count, 2,000,000; white blood count, 10,000. Nucleated red cells were more numerous, also punctate and diffuse basophilia, slight poikilocytosis, and moderate anisocytosis. Myelocytes were 1.5 per cent.

From March 21 to April 2, all stools were inspected by me. None showed signs of hemorrhage. Generally they were dark green, with some mucus and a few, soft curds.

April 6, the urine was tested for pigments, with the following results: bile pigments (Huppert's test), negative; urobilin (Schlesinger's test), negative; carotin and lactochrome, negative; hemoglobin (1) guaiac, negative, (2) spectroscope, negative.

The stool test was: stercobilin (Schlesinger's test), positive. Blood test (1) guaiac test, negative; (2) spectroscope, negative.

April 7, freshly expressed beef juice made from rare steak, and expressed juice from cooked spinach, was given alternately to the baby during breast feedings. Fowler's solution was reduced to one-half minim twice daily. The hemoglobin was 50 + per cent.; red blood count, 2,248,000; white blood count, 13,650. The platelets were greatly increased. Myelocytes were 2.4 per cent. Changes in red blood count as last noted.

April 14, the weight was 8½ pounds (3,855 gm.), and the patient looked much better. The hemoglobin was 50 per cent., and the red cell count was slowly increasing. She acted in all respects like a normal baby but was still quite pale. The spleen was just palpable at the costal margin. The liver remained normal in size.

Blood examination for reticulated red corpuscles disclosed: fresh blood mixed with 0.4 per cent. salt solution (0.8 per cent. causing crenation) containing 1 part brilliant cresyl blue in 8,000 parts of salt solution, 92 reticulated red corpuscles seen in counting 2,000 red blood cells giving a count of 46 per thousand, or 4.6 per cent. (1 per cent. or less of reticulated corpuscles is normal).

From the age of 5 weeks on, the baby progressed in health, the spleen no longer being palpable, the hemoglobin and red cell count returning to normal inside of the next few months. She was breast fed until 10½ months of age, when she weighed 19 pounds 10 ounces (8,901 gm.), and was gradually transferred to a mixed diet. Her dentition was normal and her walking and talking little if at all delayed.

When she was 3 years, 8 months old, she was 38½ inches (96 cm.) tall, weighed 36 pounds (16.3 kg.), and was bright, active and healthy.

COMMENT

The case presented shows a severe anemia in an otherwise healthy new-born infant. The anemia was so severe at 12 days of age that the patient seemed to be in danger of death from it. Examinations of the blood showed various evidences of bone marrow activity and new blood formation, such as nucleated red blood cells of both types, poikilocytes, polychromasia, stippling, and macrocytes; an increased number of platelets; while on the part of the white blood cells, myelocytes, metamyelocytes and pathologic lymphoid forms, were present.

Evidences of blood destruction such as fragmentation of red cells, achromasia and shadow forms were unobservable. The absence of jaundice, including even slight yellowness of the sclerotics, and absence of urobilin and hemoglobin from the urine, were confirmatory of lack of excessive blood destruction, so far as these signs are valid evidence. The spleen enlarged noticeably during the days when the red blood count and hemoglobin were falling, after the first transfusion.

Likewise, the spleen remained temporarily slightly enlarged following the second transfusion, but by the age of 5 weeks the spleen was no longer palpable. Blood formation was so well under way from this time on as to show steadily increasing hemoglobin and red cells and diminishing white cells. A striking and unexpected factor in this case was a normal color index. The red cells appeared to have their full quota of hemoglobin. Increase in hemoglobin continued quite as rapidly as increase in red cells, an occurrence different from what usually happens, namely, an increase in the number of red cells at a more rapid rate than increase of hemoglobin, giving a color index of less than 1.

A color index of 1 was present in this patient when the anemia was most marked at 12 days of age, and persisted while the anemia was disappearing.

The muscular twitchings of the right side present during the first three days of life, with vomiting and fever once, may have been due to intracranial hemorrhage, but there was no cyanosis or rigidity noted and the baby breathed normally and nursed well. Subsequently, no signs of cerebral damage made their appearance. If intracranial hemorrhage caused these symptoms, the amount of blood extravasated must have been small.

Ecklin [10] reported a marked but less severe anemia in a new-born infant, a comparison of which, with the case here presented, discloses many points of similarity. This case of Ecklin's is the only one which has been found, although prolonged search has been made at the Surgeon-General's Library.

Doubtless other similar cases of anemia in the new-born have occurred without finding their way into medical literature, but they can hardly be common. All of the discoverable causes of such an anemia seem to have been excluded: on the part of the mother, acute illness during pregnancy, debility, hemolytic drugs and transmissible disease; on the part of the infant, prematurity and debility, infectious diseases, hemorrhages, and jaundice both hemolytic and icterus gravis. No explanation of the cause of it can be offered. The patient's recovery was complete, and the subsequent development during three and a half years has been normal.

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[10] Ecklin, T.: Ein Fall von Anämie bei einem Neugeborenen, Monatschr. f. Kinderh. **15**:425, 1919.

ACUTE FATTY ENLARGEMENT OF THE LIVER IN INFANTS

REPORT OF FOUR CASES WITH NECROPSY EXAMINATION *

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Acute fatty enlargement of the liver after the new-born period is comparatively infrequent. During the last year we have had the opportunity of seeing four cases, the infants all being under 1 year of age. In two of these cases the etiology for the liver condition was evident; one infant had ingested some insecticide paste which contained phosphorus; in the other arsenic was the toxic agent, demonstrated after a chemical examination of the organs. In the two remaining cases the etiology was unknown; their ages were 4½ months and 11½ months, respectively. Both children were almost entirely breast fed at the time of admission to the hospital. There was nothing characteristic in the clinical history. One child had had a convulsion five weeks previously; the other had had intermittent vomiting for the last two months. On physical examination these fairly well developed children were acutely ill with a moderate rise in temperature, a mild degree of generalized icterus and a tremendous enlargement of the liver, the right lobe extending below the crest of the ilium, the lower edge of which could easily be felt on rectal examination.

Phosphorus, arsenic and chloroform are the most frequent causes of rapid fatty enlargement of the liver. The other conditions which may cause acute liver enlargement, but in which the liver rarely, if ever, reaches these tremendous proportions are (1) acute intestinal intoxication, (2) acute infection, such as pneumonia, (3) erythema desquamativum (Leiner) and pemphigus; (4) miscellaneous conditions, such as tuberculosis, syphilis and leukemia. Very obese normal infants often have a fairly large liver.

MacCallum[1] believes that the deposit of fat in the liver is one of infiltration rather than one of degeneration. Unless there is a true necrosis of liver tissue such as is found in acute yellow atrophy, fat infiltration is the better term. McNee,[2] using the old terminology,

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* Received for publication, Jan. 23, 1924.

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[1] MacCallum, W. G.: Text Book of Pathology, Philadelphia, W. B. Saunders Company, 1916.

[2] McNee, J. W.: Brit. M. J. **2**:1055, 1922.

believes fatty degeneration to be a reaction of the cells to an injury which is greater in severity than that producing cloudy swelling but less severe and slower in action than that causing actual cellular necrosis.

A marked lipemia is one of the findings which should be emphasized. In one of the cases (Case 1) the blood serum fat was over 4 per cent. This excessive fat undoubtedly has its origin in the fat depots in the body, i. e., the subcutaneous tissues. There must have been some disturbance in the fat transport. Leathes[3] has shown that this lipemia occurs only when the glycogen content of the liver is very low. Bloor[4] believes "that the cause of the lipemia is a flooding of the blood with amounts of fat greater than the normal mechanism can take care of at once." In some cases, such as acute nutritional disturbances, the liver cells receive an inadequate amount of carbohydrate and therefore must obtain and burn a much larger amount of fat to supply their energy needs; in fact, all the tissues under these circumstances must supply their energy requirements by an inordinate consumption of fat. For this purpose the subcutaneous and other fat depots are mobilized, and there is excessive fat transport as evidenced by lipemia. The liver cells and often Kupffer's cells become filled with fat. This is one method by means of which fat accumulates in the liver cells. The second method may be a diminished oxidation within the liver cell and the intracellular accumulation of fat because its rate of utilization is lower than the rate at which it is supplied. The fatty accumulation in the liver in passive congestion is another example of the latter method.

The urine in Case 1 contained glucose, the blood sugar being normal. We are unable to state the significance of this finding in relation to the fatty liver. There was no leucin or tyrosin in the urine.

In Cases 1 and 2, chemical examination of the organs failed to reveal any traces of arsenic or phosphorus; yet it is well known that even in experimental phosphorus poisoning, phosphorus cannot be found in the organs after forty-eight hours. On the other hand, phosphorus may act for a long time after the initial ingestion. Remembering that both of these children were being breast fed, it is important to know that neither one of the mothers had been taking any drugs. The other common condition of fatty enlargement of the liver such as acute intestinal intoxication, syphilis or tuberculosis can be excluded in our cases from the chemical, serologic and necropsy findings.

It has been shown experimentally[5] that the use of glucose intravenously and by mouth has prolonged the life of animals poisoned with

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3. Leathes, J. B.: Harvey Lectures, 1908-1909.

4. Bloor, W. R.: J. Biol. Chem. **49**:201 (Nov.) 1921.

5. Davis, N. C., and Whipple, G. H.: Liver Regeneration Following Chloroform Injury as Influenced by Various Diets, Arch. Int. Med. **23**:711 (June) 1919. Simonds, J. P.: The Mechanism of the Protective Action of Carbohydrate Diet in Phosphorus and Chloroform Poisoning, Arch. Int. Med. **23**:362 (March) 1919.

phosphorus. This indicates that an inadequate supply of glucose in the liver cells is responsible for the presence of increased amounts of fat as previously explained. It would therefore seem reasonable to try glucose in these cases with the possible chance of keeping the infant alive.

REPORT OF CASES

CASE 1.—*History.*—A boy, aged 4 months, was admitted to the hospital with a history of having had convulsions five weeks ago and again ten days ago. The patient was the first child and the first pregnancy, and weighed at birth 8½ pounds (3,955 gm.), at 14 weeks he weighed 12 pounds (5,443 gm.). He was breast fed entirely for six weeks and thereafter was given an occasional supplementary milk feeding. The child was perfectly well up to five weeks before admission when he had had a general convulsion lasting a few minutes. The mother attributed this to having given him a little albumen a few hours before. The child was well, gaining normally up to ten days before admission when he again had a convulsion lasting a few minutes. A lumbar puncture was made at that time which was said to have contained no cells. Since the puncture the patient had a low grade temperature, up to 102. At time of admission he was having six to seven loose bowel movements a day, and had vomited once.

Physical Examination.—The infant was fairly well developed, weighed 10 pounds (4,535 gm.) and appeared acutely ill. The skin and sclera were faintly icteric; the fontanel was not bulging. The throat, lungs and heart were normal. The abdominal examination disclosed a large smooth mass which extended below the crest of the ilium in the right axillary line and almost below to the level of the umbilicus in the left axillary line. A notch could be felt in the midline. This mass was undoubtedly the liver. Extending from under the free border of the liver in the left axillary line another mass could be felt which was probably the spleen. The lower portion of the right lobe of the liver could easily be felt on rectal examination. The temperature on admission was 106.

Laboratory Examination.—The Pirquet and Wassermann tests were negative. The urine contained a trace of albumin, a marked reaction for sugar and, miscroscopically, contained a few hyaline casts. The blood chemical examination showed a milky serum. Urea nitrogen, 11.2 mg. per hundred cubic centimeters; cholesterol, 0.436 per cent.; sugar, 0.085 per cent.; serum fat, 4.06 per cent. The Van den Bergh test for bilirubin was positive by the direct and indirect test. The blood count was, white blood cells 11,600; polymorphonuclears, 18 per cent.; eosinophils, 3 per cent.; lymphocytes, 75 per cent.; myelocytes, 2 per cent.; myeloblasts, 2 per cent. The red cells showed a mild degree of anisocytosis.

Course.—The patient's condition gradually grew worse, the temperature ranging from 102 to 105, and he died five days after admission.

Necropsy.—The infant was 23 inches (58 cm.) long with an icteric tint to the skin. The lungs were well aerated with a few small petechiae under the pleura. The heart showed no valvular defects, the muscle was pale on section. There were a few small petechiae under the pericardium. The spleen was large, weighing 19.5 gm., and was deep red on section and sprinkled with lighter spots. The liver weighed 740 gm., was mottled, pale yellow and pink. The cut surface showed pale yellowish spots, surrounded by pink areas; the section was distinctly greasy. The gallbladder was normal. The adrenals were small. The kidney cortex was pale and swollen. The Peyer's patches of the intestine were hypertrophied. The brain was wet, the vessels injected.

Microscopic Examination.—The lungs showed edema and congestion. The liver showed an intense parenchymatous degeneration and an enormous fatty infiltration of the liver cells. There were no areas of necrosis or cellular infiltration. In a frozen section stained for fat, liver cells of the inner two-thirds of the lobule were filled with fat globules; the cells of the inner one-third had less fat. Spleen: the malpighian bodies were hypoplastic. The pulp showed only moderate cellular increase and extrasinusoid congestion. The kidney showed tubular degeneration involving chiefly the convoluted tubules. Epithelial cells of the latter were swollen and the cytoplasm was transparent and hydropic in appearance. The tubules of the medulla showed slightly parenchymatous degeneration. A frozen section stained for fat showed degenerative changes in the convoluted tubules of the cortex, but no fat. Brain cells were edematous. Chemical examination of the liver showed no traces of arsenic or phosphorus.

CASE 2.—*History.*—A girl, aged 11 months, had fever for nine days. She was the first child and the first pregnancy, born at full term and breast fed up to the time of admission to hospital. For two months before admission the patient would vomit occasionally for a few days. Nine days before, she had a period of vomiting, at which time the temperature was 102. The mother was told by her physician that the baby's urine contained pus cells.

Physical Examination.—The infant was well developed, and acutely ill, with an icteric tint to the sclerae. The fontanel admitted one finger. The lips were dry, and covering the tongue, buccal mucous membrane and palate were small whitish follicles (thrush?). The lungs revealed a few coarse râles but no bronchial breathing. The abdomen revealed a large mass, probably the liver, reaching below the pelvic brim on the right side; the spleen was not palpable. There was edema of both legs. Small petechiae could be seen over the legs, left elbow and right forearm. The temperature was 103 on admission.

Laboratory Examination.—The Pirquet and Wassermann tests were negative. The urine contained no albumin, sugar or pus. It was negative for bile, leucine and tyrosin. The blood examination was, hemoglobin (Kuttner's) 75 per cent.; red blood cells, 4,400,000; white blood cells, 37,000; polymorphonuclears, 37 per cent.; lymphocytes, 60 per cent.; mononuclears, 3 per cent. There were no abnormal cells; the bleeding time was four minutes. Blood culture was negative; throat culture was negative for diphtheria. The roentgenogram of the lungs was normal. A chemical examination of medicine the child had been taking before admission was negative for phosphorus and arsenic.

Course.—The condition of the child became rapidly worse, and she died thirty-six hours after admission.

Necropsy.—Examination showed a well developed infant. The dorsum of both feet and forearm showed a few petechial spots (from 1 to 2 mm. in diameter). The thymus was not enlarged. The lungs showed a few subpleural hemorrhages and on cut section a moderate congestion. Heart showed a few precordial petechiae. The heart muscle was brown and pale. The peritoneal cavity contained 30 c.c. of clear yellow fluid. The liver was enlarged, the right lobe reached beyond the crest of the ilium. It was soft, friable and grayish-yellow, and extremely fatty. The spleen was somewhat enlarged, firm and dark red. The gastro-intestinal tract was normal; no lymphoid hyperplasia. The cortex of the kidney was of normal thickness and had a pale grayish-yellow appearance. The glomeruli did not stand out. The medulla, by contrast, had a dark red color. There was no change in the adrenals. The brain was normal.

Microscopic Examination.—The heart muscle striations were indistinct. The lungs had peribronchial round cell infiltration in places. The liver had tremendous fat infiltration through all portions of the lobules, with no area of necrosis. The spleen pulp showed congestion and cellular increase. Venous sinuses were widely dilated. The kidney showed parenchymatous degeneration of tubules with a great deal of fat deposit in the latter. The pancreas was normal, and the brain normal.

CASE 3.—*History.*—A boy, aged 5 months, had a history of cough for four days and loss of consciousness for one day. The patient was born at full term, of normal delivery. He was breast fed for one month; then on a milk mixture, and was gaining normally. Five days before admission, cough and drowsiness were noted. There was no rise in temperature. One day before admission respiration had been "grunting," and for six hours the patient had been comatose.

Physical Examination.—The patient, a well developed infant, was cyanotic and acutely ill. The fontanel was not bulging. The pharynx, heart and lungs were normal. The abdomen was lax. The right lobe of the liver reached to the brim of the pelvis. The spleen was not felt. The child died soon after admission.

Necropsy.—The heart and lungs showed no gross changes. The liver was large, extremely pale, fatty and firm; the spleen was small and soft. The stomach and intestines were normal. The kidney was small and lobulated, the capsule stripped easily; on section, it was congested with cloudy swelling. The pancreas and adrenals were normal. The brain was congested; with edema of the meninges.

Microscopic Examination.—The liver change was similar to Cases 1 and 2. A chemical examination of it revealed traces of arsenic.

CASE 4.—*History.*—A girl, aged 1 year, was admitted to hospital with a history of vomiting for three days and convulsions for one day. The family and developmental history was negative. Three days before admission the patient ingested a potato on which roach paste had been spread. The following morning (twelve hours later) the child vomited whenever fed and was drowsy. There was no diarrhea or bloody stools. The stupor increased and during the previous day she had had frequent convulsions.

Physical Examination.—A well developed child was noted, with frequent tonic spasms of the body; the pupils reacted sluggishly to light; the fundi were normal. The pharynx, heart and lungs were negative. The liver reached 6 cm. below the costal margin on the right side; the spleen was not felt.

Laboratory Examination.—White blood cells, 20,000; polymorphonuclear, 62 per cent.; lymphocytes, 29 per cent.; mononuclear, 9 per cent. The urine contained a trace of albumin, no sugar and a few hyaline and granular casts. No bile was present.

Course.—The child died a few hours after admission, with a temperature of 103.

Necropsy.—There were no petechiae, jaundice or icterus. Lungs, heart and spleen were normal. The liver was large and yellow; of normal consistency. The intestines showed small scattered areas of slight congestion of the mucosa. There were no ulcerations anywhere. Both kidneys had increased in size. On section, the cortex was normal in size, yellow in color and streaked with longitudinal red lines. The meningeal vessels of the brain were congested and the surface of the brain slightly edematous.

The heart muscle fibers were atrophic with a great deal of round cell infiltration between the fibers. The lungs showed evidences of bronchopneumonia.

The entire liver parenchyma was replaced by small and large fat droplets and some cells showed an early necrosis. This was an acute process. A fat stain showed fatty infiltration with some round cell infiltration.

The spleen showed degenerative changes of malpighian corpuscles with fatty infiltration into the centers. The stomach showed a necrosis of the mucosa.

SUMMARY

1. Four cases are presented of acute fatty enlargement of the liver in infants, with a clinical picture of severe toxemia.

2. Metallic poison should always be borne in mind as an etiologic factor in patients acutely ill that show very large livers.

3. Examination of the blood for fat may often reveal lipemia as an aid in diagnosis of fatty infiltration of the liver.

4. The administration of glucose may be of some help in treatment.

RÉSUMÉ OF THE LITERATURE FOR 1921 ON TUBERCULOSIS IN CHILDHOOD *

DIAGNOSTIC TESTS AND SEROLOGY

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Levinson[1] studied 300 children, most of whom had come in contact with tuberculosis. One hundred and forty-one reacted positively and eighty-three reacted negatively to the tuberculin test; the diagnosis of the condition of the remaining seventy-six was doubtful. Most of the children with positive reactions had become infected from the fathers. Of the group of 141 children, thirteen presented symptoms of active tuberculosis, and 128 of latent tuberculosis. Only three of those with active symptoms had active pulmonary lesions. Ninety-eight per cent. of those with latent tuberculosis had no subjective symptoms, but 90 per cent. were under weight. In 75 per cent. hilum dulness and whispered bronchophony to the seventh dorsal vertebra were present. There was a shadow in the roentgen-ray plates in the region of the hilum, and one or more calcified areas in the substance of the lung. The Eustace Smith's sign was very infrequent. Levinson believes that a positive tuberculin reaction in children should establish a diagnosis of tuberculous infection, and that the classification of this type of infection depends on the subjective and objective symptoms, and on the roentgen-ray findings.

Dietl[2] performed the Pirquet test on a number of children having symptoms suspicious of tuberculosis, and found a surprisingly small number of positive reactions. He thinks this is due to a lowered, general or cutaneous, sensitiveness to tuberculin. A positive intracutaneous test means an active tuberculosis only when small doses of tuberculin are used, and in the presence of definite lung findings. A negative reaction, however, when larger doses of tuberculin are used excludes tuberculosis.

Debré, Paraf and Dautrebande[3] have shown that a negative tuberculin test in an infant suffering from tuberculosis is owing to the fact that the test was being performed during the antiallergic period, and a diagnosis cannot be determined until a series of tests are made over a sufficiently long period of time (four months). These authors have

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* Received for publication, Feb. 26, 1924.

* Part of this material was collected by the late Dr. May Michael.

[1] Levinson, A.: Med. Rec. **99**:773 (May 7) 1921.

[2] Dietl, K.: Monatschr. f. Kinderh. **19**:422 (Feb.) 1921.

[3] Debré, R.; Paraf, J., and Dautrebande, L.: Ann. de méd. **9**:443 (June) 1921.

proved conclusively that tests made in this way cannot provoke a reaction in a healthy infant or modify the antiallergic period in a tuberculous one.

Kretschmer[4] studied the Pirquet test in 180 children under 14 years of age, with a history or clinical findings of tuberculosis. He compares his results with those of Klose and Synwoldt in the following table:

	Klose	Synwoldt	Kretschmer
Cases	120	80	180
Positive reactions (per cent.)	62.5	49	42.2
Old tuberculin reactions	9.33	1.25	28.9
Bovine tuberculin reactions	5.34	35.00	7.8
Old tuberculin greater than bovine	29.33	——	18.4
Bovine greater than old tuberculin	13.33	5.00	7.9
Bovine and old tuberculin equal	42.67	58.75	36.8

Kretschmer states that the percentage of positive Pirquet reactions among the children of Berlin is very low because of the extant malnutrition which confers immunity.

Gittings and Donnelly[5] published statistics on the Pirquet reaction, obtained from the records of the last ten years in the Children's Hospital of Philadelphia. Their results demonstrate the high percentage of tuberculous infection and the comparatively low incidence of recognizable clinical tuberculosis in childhood. The authors emphasize the importance of at least one repetition of the tuberculin test, if the first proves negative.

Furstner-Risselada[6] reports the results of the Pirquet test on 1,504 schoolchildren in Haag, a city in Holland with 360,000 inhabitants. Positive reactions were obtained in 399 children as follows: In the group of 591 children, aged 6 years, 119 positive reactions were obtained; of 278 children, aged 7 years, sixty-seven reacted positively; of 139, aged 8 years, thirty-nine gave positive reactions; of 142, aged 9 years, there were forty-five with positive reactions; of 123, aged 10 years, there were fifty-three with positive reactions; of 115, aged 11 years, there were thirty-five with positive reactions; of eighty-five, aged 12 years, there were thirty-five with positive reactions, and of thirty-one children, aged 13 years, there were six with positive reactions. These figures are much lower than those of Hamburger and Monti, probably because their patients were children in the polyclinic, whereas those observed in this study were schoolchildren chosen at random.

Salmony[7] attempted to ascertain whether localization, anemia, hyperemia, or water content of the skin had any influence on the Pirquet reaction. The tests were made on children from 6 months to 14 years of age. To determine the effect of localization, tests were made above and below the elbow joints, above the wrist, on the extensor and flexor surfaces of the forearm, and on the chest. The reaction above the wrist was least marked and the reaction of the test 5 cm. below the elbow most intensive. The Pirquet reaction was less marked when the hyperemia was produced with mustard plasters, vacuum cups or sand-bags, but was increased when produced with Bier's pump. The reaction was increased in the anemic areas. Increased moisture content of the skin was effected by the Priessnitz compress and by means of cod liver oil. Lessened water content was produced by the use of alcohol. No rule could be formulated with regard to the effect of this condition on the reaction. The author draws the following conclusions: Local factors have a decided influence on the intensity of the Pirquet reaction, but they never change the reaction from positive to negative or the reverse. Increasing the rapidity of the blood stream causes a less marked reaction, slowing the blood stream intensifies the reaction. Complete stasis of the blood stream intensifies the reaction to the greatest degree.

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[4] Kretschmer, M.: Deutsch. med. Wchnschr. **47**:465 (April 28) 1921.

[5] Gittings, J. C., and Donnelly, J. D.: Arch. Pediat. **38**:78 (Feb.) 1921.

[6] Furstner-Risselada, A. M.: Monatschr. f. Kinderh. **21**:271 (June) 1921.

[7] Salmony, L.: Arch. f. Kinderh. **69**:454 (June) 1921.

Kretschmer [8] reports his experience with the new diagnostic tuberculin, or Moro's test. This consists of old tuberculin to which is added a concentrated extract of the original culture and also bovine tuberculin. Three hundred tuberculous children, and also children in whom tuberculosis was suspected, were vaccinated by Kretschmer with this preparation. The following results were obtained: Reactions positive and similar to old, diagnostic tuberculin, 103 cases; reactions negative to both tuberculins, 131 cases, reactions more positive to old tuberculin, eighteen cases; reactions more positive to diagnostic tuberculin, twenty-four cases; reactions positive only to old tuberculin, fifteen cases; to diagnostic tuberculin only, nine cases. Kretschmer, therefore, could not see any advantage in diagnostic tuberculin over the old tuberculin.

Meyer [9] made comparative tests with old tuberculin and Moro's diagnostic tuberculin on 245 children from 2 to 14 years of age. One hundred and twenty-six children gave positive reactions. Moro's old tuberculin gave 30 per cent. positive reactions; Höchst's old tuberculin 75 per cent., and Moro's diagnostic tuberculin 98 per cent. Not only were there more positive reactions with Moro's preparation, but the reactions were more definite and the area of the erythema and induration more intense.

Brüning [10] has collected statistics in regard to the frequency of a positive Pirquet reaction on children of the well-to-do. He examined 350 children of all ages who came to him for treatment of conditions other than tuberculosis. In ninety-one, there were positive reactions.

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8. Kretschmer, M.: München. med. Wchnschr. **68**:852 (July 8) 1921.
9. Meyer, L.: München. med. Wchnschr. **68**:1286 (Oct. 7) 1921.
10. Brüning, H.: Jahrb. f. Kinderh. **96**:286 (Nov.) 1921.

Von Hayek,[11] basing his opinion on two years' experience in treating 400 tuberculous children, believes that the percutaneous injection of tuberculin, according to the method of Petruschky, gives the best results and is the easiest way of administering the tuberculin.

Korbsch[12] obtained positive cutaneous reactions with freshly drawn undiluted cerebrospinal fluid in two cases of tuberculous meningitis. Numerous controls with fluid from patients with pulmonary tuberculosis gave negative results. It is true, however, that tests with cerebrospinal fluid from patients with cerebral affections other than tuberculosis also gave positive reactions. The test could not, therefore, be regarded as specific for tuberculous meningitis.

Fischer[13] applied the intradermal tuberculin test at monthly intervals to 200 tuberculous subjects of different ages. The test was more sensitive when the diluted tuberculin was mixed with the patient's own blood serum. This test, applied to forty patients who were injected by the Mantoux technic, produced no lung, focal, or general response, but the skin reaction was a papule from 1 to 20 mm. in diameter. The skin reaction corresponded more closely to the course of the case, and seemed less dependent on the condition of the skin and location of the injection.

Dietrich[14] prepared a special tuberculin, and produced essentially different reactions with intracutaneous tests than with subcutaneous tests. He concluded that the reaction mechanism of intracutaneous tests and subcutaneous tests are essentially different.

Feer[15] describes a simple cutaneous tuberculin test in which he prepares the sterilized skin by rubbing and then applies the tuberculin.

Vitón[16] argues that occult, dormant, and masked infection with the tubercle bacillus is extremely frequent, and that most of the infections in adults are merely the transient flaring up anew of this infection acquired in early childhood. Treating the manifestations with extremely minute doses of tuberculin benefits the primary infection. As this factor disappears the other symptoms become attenuated or vanish.

Hamburger and Peyrer[17] describe the negative and positive phases of susceptibility according to Wright's opsonins. In another article[18] they discuss the negative phase of sensitiveness to tuberculin.

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[11] Von Hayek, H.: Wien. klin. Wchnschr. **33**:768 (Aug. 26) 1920; ibid, **33**:798 (Sept. 2) 1920.

[12] Korbsch, R.: Med. Klin. **17**:816 (July 3) 1921.

[13] Fischer, C.: Schweiz. med. Wchnschr. **51**:992 (Oct. 27) 1921.

[14] Dietrich, W.: Deutsch. med. Wchnschr. **47**:406 (April 14) 1921.

[15] Feer, E.: München. med. Wchnschr. **68**:1050 (Aug. 19) 1921.

[16] Vitón, J. J.: Semana méd. **28**:473 (April 21) 1921.

[17] Hamburger, F., and Peyrer, K.: Wien. klin. Wchnschr. **34**:157 (April 7) 1921.

[18] Hamburger, F., and Peyrer, K.: Wien. klin. Wchnschr. **34**:280 (June 9) 1921.

Zinsser [19] reports experimental investigation and a study of the principles of intradermal tuberculin reactions.

Kharina-Marinucci [20] performed the complement fixation test on 227 tuberculous infants. Three antigens were used, a watery emulsion, an hydro-ether-alcohol extract of the emulsion, and Koch's old tuberculin. The author examined 400 serums and concluded that the test had practically no value in the diagnosis of infantile tuberculosis.

In a later work, Kharina-Marinucci [21] reports the results of sero-agglutination tests in children. Ninety-five per cent. of 235 tuberculous children gave a positive response when the test was applied to the avian variety of tubercle bacillus. Agglutination occurred at from 1 : 25 to 1 : 100 in the majority, but in five cases at from 1 : 200. The negative responses were in the most incipient or in the most advanced cases. The titer sometimes grew higher as the child improved and lower as the disease progressed. The findings confirm those of Di Cristina, who first suggested the use of the avian variety for the purpose. The special localization of the tuberculous process did not seem to affect the response.

Ribadeau-Dumas, Cuel and Prieur [22] found, by means of the complement fixation test performed on tuberculous mothers and their infants, that women with open tuberculosis can transmit antibodies to the infant but that the antibodies disappear from the infant's blood shortly after birth.

Epstein [23] performed intracutaneous tests with the milk of tuberculous cows, and apparently confirmed the presence of a tuberculous antigen in the milk. He injected 0.1 c.c. of milk into the skin on the inner side of the forearm of children affected with tuberculosis, who had given a positive reaction to tuberculin. As a control, certified milk, milk from nontuberculous cows, and dry milk were injected into the other arm. A positive result was always obtained in tuberculous children with milk of tuberculous cows (thirty-five injections) whereas a negative result was obtained with the other milks (twenty-six injections). Epstein, moreover, showed that milk of tuberculous cows gave negative reactions when injected into children who had a negative Pirquet test. The injection of the milk of tuberculous cows frequently caused also a torpid Pirquet test to flare up and become markedly positive. From the results of these experiments the author concludes that the milk of tuberculous cows contains antigens not present in the milk of nontuberculous cows, although these antigens are not in the milk of every tuberculous cow, and the severity of the disease does not determine their presence because they occur in animals with only a positive tuberculin test as the evidence of tuberculosis.

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[19] Zinsser, H.: J. Exper. Med. **34**:495 (Nov.) 1921.

[20] Kharina-Marinucci, R.: Pediatria **29**:500 (June 1) 1921.

[21] Kharina-Marinucci, R.: Pediatria **29**:529 (June 15) 1921.

[22] Ribadeau-Dumas, M. M.; Cuel, and Prieur.: Rev. internat. de la tuberc. **2**:378, 1921.

[23] Epstein, B.: Jahrb. f. Kinderh. **95**:64, 1921.

Epstein [24] also made 1,800 parenteral injections of normal horse or sheep serum in forty-six tuberculous children, varying in age from 3 months to 14 years. He wished to study the influence of parenteral administration of foreign protein on the tuberculous organism, and the syndrome known as serum disease. He found that, contrary to the general opinion, the parenteral administration of foreign serum did not cause fever in tuberculous children, as did the injection of old tuberculin or milk. Serum reactions, however, did occur. With the administration of 10 c.c. of serum biweekly, 65 per cent. of the children had serum reactions. Severe reactions resembling shock occurred four times directly after the injection. Repeated injections caused increased sensitiveness, and the patients did not become accustomed to the injections as they did to the injections of milk and tuberculin.

In order to judge the value of the complement fixation reaction in tuberculosis, Sévi [25] tested fifty-four institutional children from 7 to 14 years of age, none of whom showed evidence of any illness. In fifty children the test was negative, in four positive. Further examination of the four who gave positive reactions revealed tuberculous lesions, and the finding was confirmed by roentgen ray.

Cook [26] has made a study of the complement fixation test for tuberculosis in children. A total of 1,855 fixation tests were performed on 1,556 children. By a careful clinical study of each case these children were separated into four groups, namely: manifest, masked, suspected and healed tuberculosis. In the first group there was no doubt concerning the diagnosis of an active tuberculosis. The results of the complement fixation test in this group show a very definite relation to the age of the child. During the first year no positive fixation reactions occurred; from 2 to 4 years about 40 per cent. of the children reacted positively to the test; from 4 to 6 years this percentage increased to 56, and above 6 years over 80 per cent. showed positive reactions. The children of the masked tuberculosis group gave positive complement fixation reactions in the same proportion as those with manifest tuberculosis. The test is consequently of great aid in calling attention to this common and frequently overlooked type of tuberculosis in children. About half of the group classified as "suspected tuberculosis" showed positive fixation reactions. Twenty patients with healed tuberculous lesions were examined. Only two of this group gave positive reactions.

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[24] Epstein, B.: Jahrb. f. Kinderh. **95**:52, 1921.

[25] Sévi, J.: Presse méd. **29**:484 (June 18) 1921.

[26] Cooke, J.: Complement Fixation for Tuberculosis in Children, Am. J. Dis. Child. **21**:78 (Jan.) 1921.

Since these children were all over 4 years of age, the results give additional evidence of the association of active tuberculosis with a positive fixation reaction. In concluding his study, Cooke points out that a positive fixation reaction is associated in a large majority of cases with a tuberculous lesion that is pathologically, if not clinically, active, and consequently, any patient giving a positive reaction should not be considered free from active tuberculosis without a thorough study.

Gibson and Carroll[27] studied the auto-urine test in forty cases of tuberculosis among children and adults. All patients with bone lesions were allergic and all reacted distinctly to the auto-urine test. No conflicting results were obtained. Every patient who was sensitive to tuberculin and had signs of active tuberculosis gave a positive auto-urine reaction. The urine of patients with active lesions, who were not sensitive to tuberculin, gave positive reactions when injected into allergic persons. Negative reactions in allergic patients bore out the opinion that they had no active lesions.

Kotzulla[28] tested fifty children to ascertain whether a positive auto-urine reaction speaks for an active tuberculosis and a negative reaction for nonactivity. He divided his material into three groups. Group 1 consisted of children free from tuberculosis or with nonactive lesions. All these gave negative reactions. Group 2 consisted of children with active lesions and these all gave a positive reaction, strong, or weak, according to the degree of activity. Group 3 consisted of children with bronchial gland tuberculosis, with positive but weak reactions. Group 4 contained children suspected of active tuberculosis, and in all of these a positive auto-urine test corresponded with the clinical evidences of activity. Kotzulla believes the auto-urine test is specific for active tuberculosis, except in cases associated with insufficiency of both kidneys, and with its aid the diagnosis of the onset of an active lesion can be made earlier than by physical or clinical methods.

Nasso[29] concludes from the results in ten nontuberculous and in fifty-three tuberculous children that the auto-urine test is specific for tuberculosis. He has simplified Wildbolz' technic in that he merely evaporates 100 gm. of urine in a broad basin at a temperature of 60 or 63 C. (140 to 145.4 F.) for three or four hours to reduce it to one-tenth of its original volume. The salts adhere to the bottom of the basin and two or three drops of the concentrated urine are injected as for the intradermal tuberculin test. Nasso also injected twenty-six children with their own serum, evaporated to one-tenth its original volume in a watch glass. He prefers this serum to the urine, as the injections are never painful and never induce necrosis, although the reaction is not quite so pronounced as with the urine.

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[27] Gibson, C. B., and Carroll, W. E.: The Auto-Urine Test for Active Tuberculosis, J. A. M. A. **76**:1381 (May 21) 1921.

[28] Kotzulla, O. H.: Ztschr. f. Kinderh. **29**:93 (April) 1921.

[29] Nasso, I.: Pediatria **29**:690 (Aug. 1) 1921.

Alexander[30] tested ninety-one patients, mostly children, for the Wildbolz auto-urine reaction. Among them were seventy-six cases of pulmonary tuberculosis, one case of cervical gland tuberculosis, one of tuberculous spondylitis, and thirteen cases in which no tuberculosis could be found. Fifteen of the patients with active pulmonary tuberculosis gave a negative auto-urine reaction; two gave, at first, a positive and later a negative reaction; and three gave first a negative and then a positive reaction. In these an improvement had occurred in the interval. In eleven patients with active pulmonary tuberculosis the test was markedly positive, in two weakly positive, and in two undetermined. In ten patients on whom the test was repeated it became more markedly positive and always so in children who were improving. The author concludes that a negative auto-urine reaction does not exclude an active tuberculosis. There is no parallelism between the intracutaneous and the auto-urine tests. The tests must be made with concentrated urine, and the best results are obtained by evaporation to one-tenth its volume in a vacuum.

Widmaier[31] calls attention to the value of the Pandy reaction in tuberculous meningitis. The test consists of adding 1 c.c. of phenol (1 part phenol crystals to 15 parts water) to 1 drop of cerebrospinal fluid. A cloudy, bluish white precipitate forms when the globulin is present in abnormal amounts. Widmaier found that the Pandy reaction was more reliable than the increased cell count, increased pressure, or pellicle formation. In cases in which the Nonne or Ross-Jones reaction was questionable this was positive. The author concludes that in all cases with blunted sensorium, convulsions, fever, and evidence of severe infections, lumbar puncture should be performed and the fluid tested for the Pandy reaction. If positive, a diagnosis of tuberculous meningitis can be made with great certainty.

PROPHYLAXIS AND IMMUNITY

Rowand[32] discusses the pathology and etiology of tuberculosis and presents a plan for the investigation of tuberculosis in childhood.

Vaughan[33] describes the sanatorium treatment and prophylaxis of tuberculosis in Detroit.

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[30] Alexander, H.: Ztschr. f. Tuberk. u. Heilstättenw. **33**:321 (April) 1921.

[31] Widmaier, E.: München. med. Wchnschr. **68**:772 (June 24) 1921.

[32] Rowand, A.: Lancet **2**:650 (Sept. 24) 1921.

[33] Vaughan, H. F.: Nation's Health **3**:625 (Nov.) 1921.

Fontes[34] gives an historical review and a plan for a general campaign against tuberculosis. He cites the gradual decline in the death rate from tuberculosis and attributes this to acquired immunity from infection early in life. In another article[35] Fontes tabulates a large number of international statistics on the prevalence of tuberculosis, commenting on inherited predisposition and inherited resisting powers. In a third paper[36] he describes "training in hygiene which will enable us to save the child of today and give him resistance for tomorrow." Fontes outlines a plan of campaign as to education, physical culture, and protection.

Jones[37] is of the opinion that from 50 to 100 per cent. of American children have tuberculous infection, and that it is the duty of the schools to find those who are likely to develop clinical tuberculosis and to give them special care. The question is, how to keep these children in school and at the same time to decrease the possibility of eventual tuberculous disease. The first step is to flag the attention of the parents; the next is to secure a complete physical examination of the child and a detailed inquiry into his mode of life. The Pirquet test is important, and the fresh air schoolroom and nutrition class most valuable aids. If the child is reached, the conversion of the parents follows automatically.

Slater[38] points out: "The chance of escaping infection is almost impossible but infection alone will not cause clinical tuberculosis. When clinical disease develops there are present both infection and a lowered resistance, neither of which alone can cause the disease. It is evident that our best means of preventing the disease is to prevent infection and build up a resistance. . . . Every means possible should be exerted to prevent infection during the first year of life. . . ."

Chadwick[39] outlines a plan which will increase the resistance of children to tuberculosis. First, the school system should be made to fit the child and not the child to fit the system. Physically subnormal children should be placed in three groups, according to the degree of physical disability. The first group should contain children only slightly subnormal, who could attend two sessions at school and need only to have their diet changed and more hours of sleep to bring them up to normal. The second group should contain children obviously underweight. They should attend only a half day session and spend the other half day out of doors. Their diet should be carefully regulated and rest must precede each meal in order to develop the appetite, for a tired child will not eat. In the third group should be children with symptoms of active disease. These should go to a sanitarium school with constant supervision. All underweight children who attend the morning session should be provided with a lunch of bread, butter and milk. School nurses are needed to follow up the children in their homes and to see that the parents realize that these children are in need of extra care to prevent the development of serious illness.

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[34] Fontes, A.: Brazil-med. **35**:344 (July 2) 1921.

[35] Fontes, A.: Brazil-med. **35**:13 (July 23) 1921.

[36] Fontes, A.: Brazil-med. **35**:98 (Sept. 3) 1921.

[37] Jones, L.: J. Mich. M. S. **20**:234 (June) 1921.

[38] Slater, S. A.: Minnesota Med. **4**:650 (Nov.) 1921.

[39] Chadwick, H. D.: Am. Rev. Tuberc. **4**: 926 (Feb.) 1921.

Bradley[40] describes the work for the prevention of tuberculosis carried out among children in Pennsylvania. At Mount Alto and Cresson, 465 tuberculous children are cared for and receive definite classroom instruction, as well as hygienic care. One hundred clinics are maintained throughout the State for the treatment of tuberculosis and for the dissemination of knowledge to prevent the spread of disease. A number of open air schools are supported for children who are known to have fever or who suffer from malnutrition.

Peyrer[41] believes that infants with positive tuberculin reactions are a source of danger in hospital wards, even if there are no tubercle bacilli found in the sputum. Older children, often with few clinical findings, occasionally have tubercle bacilli in the sputum and also are a source of infection. As the author thinks that primary infection in children, if acquired outside the family, is especially dangerous, he is particularly careful to avoid hospital infection. He believes that all hospitals should have an observation ward where newly admitted children are kept until tuberculin tests have been made and the sputum examined. After four days, children with a positive tuberculin reaction or with tubercle bacilli in the sputum can be placed in the tuberculosis ward, while others can safely be admitted to the general ward. According to Peyrer, if a child has a positive tuberculin reaction, there is no danger of reinfection.

Chadwick[42] has attempted to solve the question of malnutrition as an etiologic factor in tuberculosis by making a physical examination of underweight children in the schools of Westfield, Massachusetts. In one school of 659 pupils of all ages, he found 186 children suffering from malnutrition. Physical examinations were made of 146 children in this group and of twenty-two in the group of normal children, and 53 per cent. of the 168 gave evidence of tuberculosis of the lymph nodes and of the structures at the root of the lung. In the nine Westfield schools with 2,828 children, 32 per cent. were suffering from malnutrition, and, if the law of averages holds, fully one-third of these children had diseased bronchial nodes, the first step in the development of tuberculosis. The author believes from his study that tuberculosis and malnutrition are closely allied and questions whether malnutrition

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40. Bradley, W. N.: Penn. M. J. **24**:285 (Feb.) 1921.
41. Peyrer, K.: Arch. f. Kinderh. **69**:419 (June) 1921.
42. Chadwick, H. D.: Am. Rev. Tuberc. **5**:674 (Oct.) 1921.

may not pave the way for implantation of the tuberculous infection which is present in most children. The evidence collected confirms the belief that antituberculosis activities should be recommended more often in child welfare.

Bernard and Debré[43] emphasize the importance of separating the infant from the tuberculous mother, even if already infected, for it is prolonged, repeated infections that determine a severe tuberculosis in the infant. The authors assert that, if the infant does not die within a month of separation, the disease will probably not prove fatal. In the Laennec Hospital for tuberculous mothers the infants are taken away at once. If, after repeated tuberculin tests, they are found free from tuberculosis, they are placed in private homes. If they are already infected, they are kept under observation to determine the degree of the infection. A child with active tuberculosis is kept in the hospital and the disease usually proves fatal. Infants with a positive cutaneous reaction and symptoms on the part of the gastro-intestinal tract, are given mother's milk and kept in the fresh air until it is proved that the disease is latent; then they are sent either to a crèche or are boarded out in private families.

Köffler[44] has studied the significance of reinfection with the tubercle bacillus. Animal experimentation has taught that a tuberculous infection causes a relative immunity from reinfection with small numbers of bacilli but is no protection against massive infection. On the other hand, animals show a sensitiveness to reinfection with massive doses. Köffler gives tables which show that this is true also in man. His first table shows a number of families, one of whose members has a large number of tubercle bacilli in the sputum. All the children, except those of one family of three, reacted to tuberculin, and all, except two older children, were markedly sensitive to tuberculin. In the second table, illustrating families one of whose members occasionally has tubercle bacilli in the sputum, the children were very slightly sensitive to tuberculin. As to the fate of the children in the two groups, it was found that there was a much higher percentage of severe cases, hence a higher mortality, among the younger children of the first group, but there was practically no difference in the morbidity or mortality among the older children of the two groups. The author believes that reinfection has, then, far less significance than primary infection.

Köffler[45] also reports the results of his investigations on infection among the members of families in which tuberculosis is present. He worked among children from the clinic, the infant welfare and tuberculosis consultation, dividing them into three groups: Group 1, composed of eight families, one of whose members had numerous tubercle bacilli in the sputum and many moist râles over the lungs. All the children of these families reacted to tuberculin, with the exception of three infants. Group 2, composed of nine families, whose affected member had only a few tubercle bacilli in the sputum; of the twenty-nine children of these families, fourteen were infected. Group 3, families in which some member had clinical tuberculosis but no tubercle bacilli in the sputum. A point of interest was that of the thirteen infants in the three groups only three gave a positive tuberculin reaction and only one of the four infants was in the first group, that which contained a patient having numerous tubercle bacilli in the sputum.

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[43] Bernard, L., and Debré, R.: Paris méd. **11:**27 (Jan. 1) 1921.

[44] Köffler, T.: Arch. f. Kinderh. **70:**95 (Oct.) 1921.

[45] Köffler, T.: München. med. Wchnschr. **68:**1172 (Sept. 16) 1921.

The author draws the following conclusions from his study: A patient expectorating sputum containing tubercle bacilli will infect all the children in the family, but infants under 1 year of age often show no reaction, in spite of every opportunity to become infected. Patients whose sputum contains only a small number of tubercle bacilli are much less infectious. Patients who have no tubercle bacilli in the sputum are not infectious. Patients with grave clinical pulmonary tuberculosis, with occasionally profuse bloody sputum, are exceedingly dangerous to children. Children over 1 year of age are always infected, if there is abundant and long continued opportunity. These children become ill as the result of the first infection and present a high mortality. Young children in families of patients, who have only a few tubercle bacilli in the sputum, do not show such a tendency to acquire tuberculous disease. Children over 2 years of age, though opportunity is given, do not become infected so often as younger children, and the mortality is lower. Children of patients who eliminate large quantities of bacilli are, on account of constant reinfection, highly sensitive to tuberculin.

Stuhl[46] is of the opinion that, if the infant is not taken away from the tuberculous mother, the mother should nurse the child. He thinks the passage of antibodies from mother to infant by the milk has been proved by animal experimentation and that these produce a passive immunity. Daily examples of infants who have escaped infection when nursed by their tuberculous mothers also prove that the milk contains antibodies. The author believes, too, that the number of antibodies in the milk can be increased by treating the mother with tuberculin during pregnancy and lactation.

Cargin[47] laments the lack of control over the milk supply in England. He cites the high incidence of tuberculosis, human and bovine types, and says: "Apart from the infection of the human body with the bovine bacillus, when it is considered that the number of deaths from tuberculosis in the first year of life is probably much higher than one in twenty-six (Sir A. Newsholme), and that the total deaths from this disease in England and Wales amounts approximately to 50,000 per annum, it will be agreed that the most stringent regulations are urgently necessary to enable infected and diseased animals to be disposed of without delay."

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[46] Stuhl, C.: Med. Klin. **17**:315 (March 13) 1921.

[47] Cargin, H. M.: Brit. M. J. **2**:894 (Nov. 26) 1921.

Blatt,[48] recording observations on the physical development of tuberculous children, takes two groups for the basis of his study: a control group of 614 children who showed no evidence of tuberculosis and whose parents were free from the disease, and a group of 508 children with suspicious or positive evidence of tuberculosis, whose parents were tuberculous. The necessity for a control group of children of the same social status and living in a similar environment was shown by a comparison of the control group with the ideal weights given by the Children's Bureau of the Department of Labor. Blatt's statistics of the initial weight and height show that the weight in the control group reached that of the Children's Bureau standard more frequently than did the weight of the tuberculous group; but the height in the tuberculous group reached that of the Children's Bureau standard before that of the control group. The tuberculous child is the tall, lanky one.

The children of the two groups were observed over a variable period of time. The minimum average period for the boys was fourteen months and the maximum fifty-one and one-half months; for the girls the minimum was nine months and the maximum sixty-nine months. After this period of observation the children in the tuberculous group attained the normal standard of height and weight more frequently than did those of the control group, although the children of neither group reached the standard of the Children's Bureau. The superiority of the children of the tuberculous group over those of the control group Blatt believes due to improvement in sanitation, food, and the removal of defects.

Von Ruck and Flack[49] add another contribution to their previous reports on vaccination of children against tuberculosis. A total of 3,000 children have been vaccinated since 1903, and not a single case is known, according to the authors, in which the tuberculosis recurred or became active. The time intervening since the vaccination has, however, been too short to draw final conclusions. If vaccination is not resorted to during the first years of life, infection is already accomplished. Since in about 70 per cent. of the cases infection had already taken place, the authors cannot regard their work as a strictly prophylactic measure against tuberculosis but one against "consumption." Children in a tuberculous environment should be vaccinated at birth; but every child should be vaccinated, and the earlier it is done the better are the prospects that no tuberculous infection will occur.

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[48] Blatt, M. L.: The Physical Development of Tuberculous Children, Am. J. Dis. Child. **21**:575 (June) 1921.

[49] Von Ruck, K., and Flack, R. E.: M. Rec. **99**:1048 (June 18) 1921.

Shiga [50] has attempted to immunize children threatened with tuberculosis and to treat early forms. He uses a serovaccine in six different dilutions: from 1 : 5000 to 1 : 100. The sixth solution consists of virulent, living tubercle bacilli from 1 : 20, of which, at first, 0.2 c.c. and then 1.0 c.c. are injected. The author has treated in the last four years 300 ambulatory cases of tuberculosis and has given the vaccine as a protective measure in twenty cases. His results are satisfactory.

Jaenicke [51] believes that the Petruschky percutaneous method of prophylaxis of tuberculosis in children is of value.

Montenegro [52] made four intradermal tests with each of three partial antigens in twenty-four children before and after a three months course at a seashore sanatorium. Along with general improvement in the active group, the reactions were always intensified. He believes that the reaction to the partial antigens of the tubercle bacillus is much more instructive than the reaction to any "whole" tuberculin.

Cozzolino [53] agrees with Peyrer that tuberculous infants are a source of infection even if there are no tubercle bacilli in the sputum. He cites the instance of a tuberculous infant with a negative sputum who infected two older sisters.

Wallgren [54] experimented with rabbits and found that young animals are not less resistant to infection than older animals. He thinks this may be true in the human being also, and that the fact of manifest tuberculosis in infants and young children being rapidly fatal is due to a massive infection. Clinical evidence, therefore, as to the gravity of tuberculosis in infancy does not necessarily indicate that the resistance in infancy is less than in childhood or adult life.

Ickert [55] reports that in 939 homes where tuberculosis was present the contagious member of the family was isolated in the house in 536 instances, away from the house in seventy cases, and in 103 the children were removed from the home.

ETIOLOGY AND PREVALENCE

Krause [56] does not believe that the only mode of tuberculous infection in childhood is direct contact with tuberculous patients. He believes that infection from dried sputum must be seriously considered. Indoors, the sputum bespatters the floor where children are playing. Out of doors, the children engage in ground games and contaminate their hands with the dirt of the sidewalks and streets, containing dried sputum from many persons. There are few children who do not put their fingers in their mouths, thus completing the chain of transmission.

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[50] Shiga, K.: Internat. J. Pub. Health. **2**:34 (Jan.-Feb.) 1921.

[51] Jaenicke, C.: Ztschr. f. Tuberk. u. Heilstättenw. **33**:265 (Feb.) 1921.

[52] Montenegro, V.: Arch. Espan. de Pediat. **5**:65, 1921.

[53] Cozzolino, O.: Pediatria **29**:633 (July 15) 1921.

[54] Wallgren, A.: Tubercle **2**:481 (Aug.) 1921.

[55] Ickert, F.: Ztschr. f. Tuberk. u. Heilstättenw. **34**:355 (June) 1921.

[56] Krause, A. K.: New York State J. Med. **21**:83 (March) 1921.

Ribadeau-Dumas[57] believes that tuberculosis in infancy is nearly always the result of inhalation of the tubercle bacillus. The primary lesion is found most frequently at the bases of the lungs and is usually a single tuberculous nodule with miliary tubercles in the neighborhood. If active, there is an area of caseous degeneration, surrounded by a zone of congestion, which sometimes involves the entire lobe of the lung and resembles a pneumonia hepatization. The latent stage is seen in older children when the primary lesion consists of encysted, fibrocaseous tubercles, often calcified. The active process, according to the author's observation, occasionally starts in these old cicatrized areas, but as a rule shows no sign of activity even when the lung is the seat of an active secondary process. From the primary focus the hilum glands become involved, then the apices of the lungs. Apical lesions tend to spread more extensively, and are more serious than the primary hilum lesions.

TABLE 1.—*Children Found to be Infected with Tuberculosis Among Those Subjected to the Pirquet Test*

Age.	1912-1914 (600 Children) Per Cent.	1914-1916 (658 Children) Per Cent.	1916-1918 (638 Children) Per Cent.	1919 (271 Children) Per Cent.	1920 (249 Children) Per Cent.
1 - 3 months	0.0	2.4 (41)	4.7 (43)	0.0 (16)	2.9 (35)
4 -12 months	5.0	7.8	9.4 (85)	17.0 (48)	4.2 (48)
1 - 2 years	12.0	23.0	26.0 (74)	11.0 (35)	17.6 (34)
3 - 4 years	32.0	25.0	52.0 (96)	29.0 (47)	39.2 (28)
5 - 6 years	33.0	50.0	51.5 (66)	57.5 (33)	47.6 (21)
7 -10 years	47.0	56.0	43.5 (163)	47.0 (57)	57.5 (40)
11 -14 years	56.0	66.0	60.0 (111)	63.0 (55)	60.4 (43)

Van Zwaluwenburg and Grabfield[58] have collected evidence which they believe points to an intimate relation between the occurrence of tubercles in the faucial tonsil and the so-called pleural cap. The pleural cap is a shadow seen in roentgen-ray plates which occurs along the surface of the second rib and is separated from the shadow of the second rib by a clear space from 3 to 4 mm. wide. The study of consecutive sets of plates on the same individual taken at considerable intervals, established certain definite progressive changes in the development of this shadow with the lapse of time. The writers examined with roentgen ray the chests of sixteen persons who had tuberculous lesions in their tonsils. All but one showed the pleural cap. The chests of

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57. Ribadeau-Dumas, L.: Les Tuberculosis de l'Enfant et de l'Adulte, Paris, Maloine et fils, 1921, **17**.

58. Van Zwaluwenburg, J. G., and Grabfield, G. P.: Am. Rev. Tuberc. **5:**57 (March) 1921.

seventy-seven patients whose extirpated tonsils were found free from tuberculosis were also examined. Three disclosed a pleural cap while twenty-four did not.

Peyrer [59] reports two cases which illustrate the malignant course that tuberculosis may run in older children.

Between January 1918 and October 1920, Sander [60] examined 992 children of the city of Dortmund in order to ascertain whether tuberculous infection had increased since the war. He found that among children aged 2 years, hardly 6 per cent. were affected, and among those from 5 to 6 years of age only 19 per cent., whereas at this age in other cities the average is 90 per cent.

Ickert [61] has collected mortality statistics on tuberculosis in children and youths during the years of the war. He found the mortality increased in Germany and in Holland, in the former ten times more than in Holland. This increase did not affect all ages equally. For young children it was 100 per cent., for schoolchildren 50 per cent. and for young adults 200 per cent. During school age, because of specific immunity, there is less danger to life and a greater tendency for the tuberculous process to heal.

TABLE 2.—*Percentage of Infected Children Who Exhibited Clinical Tuberculosis, and Percentage of Mortality Among the Latter*

	1912-1914		1914-1916		1916-1918		1919		1920	
Age.	Tuberculosis, per Cent.	Deaths, per Cent.	Tuberculosis, per Cent.	Deaths, per Cent.	Tuberculosis, per Cent.	Deaths, per Cent.	Tuberculosis, per Cent.	Deaths, per Cent.	Tuberculosis, per Cent.	Deaths, per Cent.
1 year............	100	80	70	77	60	67	75	50	66	50
2 - 4 years..	0.5	21	66	58	54	67	55	40	47	12.5
5 - 6 years...........	0.4	20	35	61	32	45	47	33	70	33
7 -10 years...........	32	7	32	40	29.5	33	41	36	39	44
11 -14 years...........	28	6	27	14	12	10	14	33	15.4	0

Umber [62] presents exact statistical data which concern 2,416 children who were treated at the Municipal Hospital of Charlottenburg, Berlin, during the years from 1912 to 1920. Only those children have been listed as nontuberculous who remained negative to the Pirquet test after repeated application. It will be seen from these figures that, whereas in the years before the war no infants from 1 to 3 months were found to be infected, this was no longer the case after the outbreak of the war.

Examination by Schram [63] of 500 children under 9 years of age from homes where tuberculosis existed showed that 80 per cent. gave a positive tuberculin reaction. Among 168 children in homes where tuberculosis was particularly contagious, positive reactions were obtained in 100 per cent. of children over 5 years of age. Schram feels that it is impossible to protect children in such homes.

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[59] Peyrer, K.: Beitr. z. Klin. d. Tuberk. **47**:164, 1921.

[60] Sander: Deutsch. med. Wchnschr. **47**:532 (May 12) 1921.

[61] Ickert, F.: Ztschr. f. Tuberk. **34**:7 (April) 1921.

[62] Umber, F.: Ztschr. f. Tuberk. **33**:257 (Feb.) 1921.

[63] Schram, T.: Norsk. Mag. f. Laegevidensk. **82**:740 (Oct.) 1921.

Hempelmann[64] states that: "Infection with the tubercle bacillus usually takes place sometime after birth from exposure to another individual who is suffering from the disease, or from an infected milk supply. . . . The mortality among infants is 78.7 per cent. during the first year of life and 57.4 per cent. between the ages of 1 and 2 years."

Hamburger,[65] in estimating the prevalence of tuberculosis, urges that children in schools and contagious diseases hospitals be selected rather than child patients in dispensaries.

LESIONS

Oldenburg[66] relates that of the 130 children under 4 years of age with pulmonary tuberculosis at the sanitarium in his charge, 53 per cent. were dismissed much improved or cured, and 64 per cent. of the 105, with an interval up to six years, have been in average good health since; 20 per cent. died, and no information could be obtained in regard to 16 per cent.

Zimmermann[67] has made a study of the frequency of severe pulmonary tuberculosis in 333 children, and found that apparently cases of severe pulmonary tuberculosis in children are more frequent than they formerly were. In a previous study, 12 per cent. of the severe cases were fatal, in this study 25 per cent.

Barchetti[68] had under observation for from two to four years fifty-one infants of tuberculous mothers. Of these, fourteen remained free from tuberculosis, thirty-seven showed evidences of the disease. Of the thirty-seven tuberculous infants, eleven were discharged clinically well and twenty-six died. Of the fourteen infants who did not contract the disease, eleven were less than 6 months old and four were in the second half of their first year. Of the eleven patients discharged as clinically well, seven were examined later and gave no evidence of tuberculosis.

Opie and Anderson[69] state that: "The lesions which occur in the lungs of almost all individuals who die from conditions other than tuberculosis have the characteristics of the tuberculosis of childhood, that is, they occur as foci in the substance of the lung and are not more frequent in the apices than elsewhere. They are accompanied by more extensive lesions in the adjacent lymphatic nodes. The occurrence of these focal lesions, which are almost constantly found, does not exclude the more familiar type of tuberculosis, namely, the apical lesion. In association with the apical lesions, which occur in the later period of childhood and in adult life, there is no caseation nor calcification of the regional lymph nodes. . . . Apical lesions increase in frequency with increasing age." They rarely occurred before 10 years of age; from 10 to 18, the incidence was 11 per cent., between 18 and 50 years of age, the incidence of apical lesions was much increased, for they were present in more than one-third of those who had died from all causes.

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[64] Hempelmann, T. C.: Internat. Clin. **2:**143, 1921.

[65] Hamburger, F.: Norsk. Mag. f. Laegevidensk. **82:**294 (April) 1921.

[66] Oldenburg, T.: Ugesk. f. Laeger **83:**683 (May 26) 1921.

[67] Zimmermann: Ztschr. f. Kinderh. **28:**59 (Feb.) 1921.

[68] Barchetti, K.: Monatschr. f. Kinderh. **21:**563 (Sept.) 1921.

[69] Opie, E. L., and Anderson, Hans: Am. Rev. Tuberc. **4:**629, 1921.

Simon [70] has for a number of years turned his attention to the study of the primary forms of tuberculosis in children. He was able to demonstrate the focus in roentgen-ray plates in thirty-six cases. In twenty-four of the cases the lesion was single. In instances of a single lesion the right side was involved three times as often as the left. That the lesions of the left side are not found so frequently is owing to the fact that the cardiac shadow hides a large part of the pulmonary field. Only rarely were the hilum changes limited to the side of the primary focus. Clinical diagnosis of the primary focus is impossible without the roentgen ray. Clinical findings always depend on hilum changes, except in very young children.

Gruber [71] found, in a series of necropsies on twenty-five soldiers (Senegal-African) who died from pulmonary tuberculosis, pulmonary and glandular tuberculous lesions similar to those found in European children. This testifies, Gruber believes, to unpreparedness, the defencelessness of those exposed to infection for the first time, and confirms the fact that tuberculosis in adults is, in the fullest sense of the word, a children's disease.

Alesandrini,[72] on the basis of radiologic examinations, which were controlled by clinical observations and necropsy findings, denies that apical infection in adults is due to a primary infection in childhood. The primary focus is usually in the lower lobes and extends outward from the hilum.

Vis [73] studied the localization of tuberculous lesions in children. He believes that the hilum is the most frequent site of clinical tuberculosis for two reasons. The infant has little or no immunity to the tubercle toxin, and offers only slight resistance to the development of

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70. Simon, G.: Ztschr. f. Tuberk. u. Heilstättenw. **34**:345 (June) 1921.

71. Gruber, G. B.: Ztschr. f. Kinderh. **28**:243 (March) 1921.

72. Alesandrini, P.: Policlinico **28**:1 (Jan.) 1921.

73. Vis, W. R.: Apex, Hilum and Lower Lobe Lesions of Tuberculosis in Childhood, J. A. M. A. **76**:1156 (April 23) 1921.

the infection. The lymphatics carry the infection to the nearest lymph gland and then to the other glands in the chain. Thus an early involvement of the hilum is inevitable in most cases. From personal observation and from statistics obtained in the literature, the writer believes that in children apex involvement is more common than lower lobe involvement.

St. Engel[74] has for a number of years studied the so-called epituberculous pulmonary tuberculosis described by Eliasberg and Neuland, and, on the whole, his conception of the disease coincides with that of the latter authors, but he prefers the term paratuberculous infiltration because the infiltration surrounds and is not implanted on the tuberculous focus. The onset in St. Engel's cases was more rapid than it was in the cases described by Eliasberg and Neuland and fever was present. Otherwise, the symptoms were similar. The roentgen ray substantiated the physical findings and showed that the infiltration was not limited by the pulmonary fissure. The disease in St. Engel's cases ran a chronic course, but finally all signs disappeared and the shadows on the roentgen-ray plate gradually cleared from periphery to hilum. This favorable outcome shows that the disease itself is not essentially tuberculosis but possibly pneumonia in the presence of tuberculous infection. Necropsies in three cases confirmed this supposition. Tuberculous changes occurred in the glands but not in the chronic thickened pulmonary tissue, and the infiltration was always on the same side as the tuberculous glands. Gravinghoff[75] believes that the work of Eliasberg and Neuland on epituberculous infiltration is a step forward in the knowledge of chronic pulmonary disease of childhood. He has made a careful study of four cases and concludes that, although the condition is not very common, it should be given further consideration and study. In one of his cases which came to necropsy, Gravinghoff found no evidence of tuberculosis.

Greenberg[76] calls attention to a type of tuberculosis in children which he calls chronic tuberculous hilum pneumonia. He defines it as a diffuse or parenchymatous process involving the portion of the lung immediately adjacent to the hilum, characterized by a gradual onset, comparatively mild constitutional symptoms, and fairly definite physical signs. As a rule, the disease ends in recovery, even in children under 2 years of age.

Eliasberg and Neuland[77] describe in detail gelatinous infiltration of the lungs in children and differentiate it from epituberculosis infiltration.

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[74] St. Engel: Berl. klin. Wchnschr. **58**:877, 1921.

[75] Gravinghoff: Monatschr. f. Kinderh. **21**:447 (Aug.) 1921.

[76] Greenberg, D.: Chronic Tuberculous Hilus Pneumonia in Children, Am. J. Dis. Child. **21**:65 (Jan.) 1921.

[77] Eliasberg, H., and Neuland, W.: Jahrb. f. Kinderh. **94**:102, 1921.

The acute onset and the rapid spread of the process over the entire lobe seem to point to rupture of tuberculous material into one of the pulmonary vessels. The onset and the course of the disease differ materially from epituberculous infiltration with its gradual onset and tendency to end in recovery. Three symptoms of gelatinous infiltration are always lacking in epituberculous infiltration, namely, high temperature, involvement of other parts of the lungs, as revealed by the roentgen ray, and the presence of tubercle bacilli in the sputum. The general condition of the children differs greatly in the two conditions.

Siegel[78] describes four cases of pulmonary tuberculosis in young children brought to the hospital with minor complaints, or with a diagnosis other than tuberculosis. He details the differential diagnosis.

Schott[79] describes a very unusual form of pulmonary tuberculosis under the name of "honeycomb" lung. The patient, an 8 months old infant, was brought to the hospital after a few months of paroxysms of coughing and vomiting. Examination showed slightly impaired resonance with faint breath sounds over the lower lobe of the right lung, and a few bronchial râles scattered over the left lung. Later, the impairment over the right lung became more marked. The tuberculin and blood Wassermann reactions were negative. The child died with symptoms of cyanosis and dyspnea. At necropsy there was found a widespread and unusual form of phthisis of the right lung. On section the entire lower lobe and part of the middle lobes were found honeycombed with cavities separated by thickened pulmonary tissue. The cavities varied in size from a pinhead to a bean. Some were filled, others were empty. Blood vessels could be seen, but no bronchi. From the microscopic examination it was determined that the cavities were not the result of a bronchiectasis, but were *ectasis infundibulae,* that is, dilatations of the part of the respiratory tract still partly lined with cylindric epithelium. The walls of the cavities consisted of a thin layer of tuberculous granulation tissue in which were cells of various kinds, epithelial and plasma, a few leukocytes, and typical giant cells containing tubercle bacilli. No explanation was given as to the manner in which these cavities were formed.

Schoenstein[80] reports a case of pneumothorax in an 8 months old infant. The diagnosis was made with the roentgen ray during life. Necropsy revealed a tuberculous cavity which had ruptured into the pleura.

Bourne[81] reports a case of complete pneumothorax in an 18 months old infant. He finds it interesting for two reasons: first, because of the extreme rarity of the condition, and second, because it sheds some light on a probable mode of transmission of the tubercle bacilli to the lungs in childhood. The patient was admitted to the hospital with a temperature of 102 degrees, cyanosis, cough, and dyspnea. He had been well until three months before, when he had an attack of measles, after which there was loss of appetite, constipation, emaciation and cough. The cyanosis had developed only a few days before entrance. Examination of the chest revealed a complete pneumothorax of the left side and a bronchopneumonia of the right lung. The child died, and at necropsy the left lung was found completely collapsed, except at the apex where it was adherent to the pleura. The left parietal pleura was studded with tubercules, as was also the left lung. At the apex of the lung was a cavity which communicated by a small rent with the left pleural cavity; in the right lung were many tubercles. The hilum glands were only slightly enlarged and not caseous. The mesenteric glands, on the other hand, were enlarged and caseated. The liver, spleen and kidneys contained numerous miliary tubercles.

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[78] Siegel, A. E.: New York M. J. **114**:223 (Aug. 17) 1921.

[79] Schott, A.: Beitr. z. Klin. d. Tuberk. **48**:112, 1921.

[80] Schoenstein, E.: Pediatria **29**:535 (June 15) 1921.

[81] Bourne, G.: Brit. M. J. **1**:526 (April 9) 1921.

Gloyne [82] says there are three ways in which the tubercle bacilli may reach the bronchomediastinal glands: (1) by direct drainage from the lung parenchyma, bronchioles, and subpleural tissue; (2) by anastomosis between the mediastinal lymphatic vessels and those of the thoracic duct or those of the cervical glands, and (3) by direct blood infection through branches of the pulmonary or bronchial arteries. In order to study further the pathology of mediastinal glands, at necropsy Gloyne dissected out all glands in five tuberculous and three nontuberculous patients. The average number found in the eight cases were: tracheal, nine; interbronchial, thirty-five; bifurcation, five; superior mediastinal, ten. The mediastinal and cervical glands were found microscopically to contain tubercles, although none could be detected by the naked eye. There was not sufficient variation in the severity of the microscopic lesions to demonstrate the course of the tuberculous infection along the chain of mediastinal glands. Roentgenograms of glands showing calcareous nodules were readily distinguishable from those showing anthracosis, caseation, microscopic deposit of tubercle, or malignant disease, by their extreme density and the sharp outline of the shadows produced by calcareous deposit.

Méry [83] also believes it very important to know the manner of dissemination of tuberculosis from the tracheobronchial glands. He says this occurs by means of the circulation, bacillemia, by rupture of the gland into a bronchus, and by direct extension.

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82. Gloyne, S. R.: Tubercle **2**:300 (April) 1921.

83. Méry, H.: Presse méd. **29**:313, 1921.

Frischman[84] calls attention to the well established fact that tracheobronchial tuberculosis follows focal pulmonary infection in childhood, and that lesions in the tracheobronchial glands are larger and more common than pulmonary lesions.

Rüscher[85] has made a study of thirty cases of bronchial asthma in children, with the idea of ascertaining whether there is any relation between this condition and tuberculosis of the bronchial glands. Sixteen of the cases gave a negative and fourteen a positive reaction to tuberculin. Almost all the children showed more or less marked evidence of the so-called exudative diathesis.

Laborderie[86] describes the roentgen-ray picture of enlarged tracheobronchial glands. In concluding his article, the author emphasizes the importance of the roentgen ray not only in the diagnosis but also in the treatment of enlarged tracheobronchial glands.

Thiers[87] studied tuberculous bacillemia in children. Her observations were made on twelve cases of tuberculosis, which included four cases of meningitis, two of Pott's disease, one of acute disseminated tuberculosis, one of tuberculous adenitis, two of ulcerocaseous tuberculosis, one of pleuroperitoneal tuberculosis, and one of ulcerocaseous peritonitis. The blood was obtained from one of the veins in the elbow or from the external jugular vein, treated with acetic acid and a strongly alkaline solution of sodium hypochlorite (antiformin), and injected into guinea-pigs. Positive results were obtained in three cases only, one of acute disseminated tuberculosis and two of Pott's disease. Thiers believes that the search for tubercle bacilli in the blood should always be made on the living child, that the finding of the bacilli after death is of no significance, because there is a necropsy arrest of the organisms in the blood and viscera. Tubercle bacilli are more frequently found in the blood four or five days before death, never forty-eight hours before or on the same day. Bacillemia, then, is evidently a variable and transitory phenomenon, the bacilli appearing in the blood and again disappearing rapidly. This explains the contradictory results of different authors. Negative results show only that the bacilli were not there at the time the search was made, or that the experiment was unsuccessful. They do not show whether they were present before the test or will appear later. Positive results are evidence of a bad prognosis.

Wollstein and Spence[88] report that of 8,919 sick children admitted to the Babies' Hospital in New York, 4 per cent. had symptoms of tuberculosis in some form. In three cases lesions were found at necropsy that had not been suspected during life. They believe that there is a greater incidence of tuberculosis of infants and young children acquired by inspiring tubercle bacilli than there is of that acquired by swallowing bacilli with food and milk. There is a rapid generalization of tuberculosis in young subjects, the rapidity and degrees of generalization being, as a rule, in inverse proportion to the age. Terminal meningitis is common. There were no cases of healed tuberculosis in 184 necropsies.

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[84] Frischman, L.: New York M. J. **114**:634 (Dec. 7) 1921.

[85] Rüscher, E.: München. med. Wchnschr. **68**:1155 (Sept. 9) 1921.

[86] Laborderie, J.: J. de radiol. et d'electrol. **5**:113 (March) 1921.

[87] Thiers, G.: Thésè de Paris, 1921.

[88] Wollstein, Martha, and Spence, R. C.: A Study of Tuberculosis in Infants and Young Children, Am. J. Dis. Child. **21**:48 (Jan.) 1921.

Wimmer [89] cites the case of a boy, aged 11 years, healthy except for transient gastric disturbances, who developed acute miliary tuberculosis with delirium and extreme dyspnea. Death occurred in less than two weeks. There had only occasionally been fever during the brief course of the disease, and nothing to explain the dyspnea on auscultation.

Pestalozza [90] examined at necropsy the pancreas in sixty cases of tuberculosis among children. In nine instances there were evidences of tuberculosis, either disseminated miliary tuberculosis or large tuberculous infiltrations. In all the others there were sclerotic changes. The author is of the opinion that connective tissue proliferation is a constant accompaniment of tuberculosis in childhood.

Kleinschmidt [91] has seen few children with phlyctenular conjunctivitis who did not react to repeated Pirquet or intradermal tuberculin tests. He thinks that tuberculosis is a very significant factor in the etiology of this condition, but cannot affirm that it is always the only factor, for even when the children react to a tuberculin test, only a few have tuberculous disease and the others have healed foci. He is inclined to lean toward the teachings of Czerny, who believes that phlyctenular conjunctivitis has an endogenous cause, namely, a constitutional anomaly, the exudative diathesis, and that the exciting cause is some toxin. The tuberculotoxin is the most important, but other toxins, such as those of measles, may play a rôle.

Guillery [92] found that by intravenous injections of tuberculin or by the instillation of tuberculin into the eyes of tuberculous animals, previously treated with tuberculin, he could produce lesions similar to phlyctenules. He obtained the same reaction with staphylococcic toxins. Guillery believes that this shows that phlyctenular disease is a nonbacillary tuberculid, caused by the action of the toxins.

Barney [93] believes that cases of genital tuberculosis in children are often overlooked, or ascribed to an infection by organisms other than

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89. Wimmer, L. K.: Semana med. **28**:426, 1921.
90. Pestalozza, C.: Clin. pediat. Modena **2**:261, 1920.
91. Kleinschmidt, H.: Beitr. z. Klin. d. Tuberk. **48**:188, 1921.
92. Guillery: München. med. Wchnschr. **68**:201 (Feb. 18) 1921.
93. Barney, J. D.: Genital Tuberculosis in Male Children, Am. J. Dis. Child. **22**:565 (Dec.) 1921.

the tubercle bacillus. He analyzed eleven cases, the total found in the records of the Massachusetts General Hospital from 1872 to July 1921. The epididymis was affected in all the cases, but bilateral infection was found less commonly than among adults. It occurred in only one case at the time of the patient's entrance to the hospital. In another, the second side became involved twenty-seven months after the removal of the epididymis first affected, in a third case three months after removal. In the other eight patients the disease occurred equally on the right and left sides.

Tuberculosis of other parts of the genital region was found less frequently in children than in adults. In only one of the eleven cases were the kidneys affected. The primary focus of genital tuberculosis can usually be demonstrated by the roentgen ray in the lung or in the bronchial nodes. In the author's eleven cases there was evidence of pulmonary tuberculosis in five cases, of tuberculous peritonitis in two, of tuberculous otitis in two, of bone tuberculosis in two, and of cervical adenitis in one.

Zerbino [94] cites a case of tuberculous orchitis and epididymitis in a boy, aged 5 years, following trauma of the region. The tuberculous process had apparently healed after several months of heliotherapy, but flared up anew during an attack of measles and apparently subsided again. Zerbino calls attention to this temporarily mild form of genital tuberculosis in children and the danger of an exacerbation during puberty.

Curchod [95] describes Hutinel's disease (tuberculous cardiohepatic cirrhosis), and reports three cases, two in children. In early childhood the onset of the disease is usually with bronchitis or pleurisy. In the course of months enlargement of the liver, ascites, and disturbances in the general circulation develop. Examination of the heart fails to disclose a pericarditis or any lesion sufficiently severe to explain the evidences of decomposition. The chief sign is the immobility of the apex, which is adherent to the chest wall. The edema is characteristic in that it begins first in the face, then in the hands and feet. At necropsy cirrhosis of the liver, tuberculous pericarditis, pleurisy, adhesive mediastinitis, and subphrenic peritonitis are found.

In the last few years Hutinel and Merklen [96] have encountered more than twenty cases of tuberculous meningitis in children suffering from hereditary syphilis. They think that syphilis favors the location of tuberculosis in the meninges. Among 206 patients with tuberculous meningitis there were twenty-three with manifestations of syphilis, and

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94. Zerbino, V.: Arch. latino-am. de pediat. **15**:317, 1921.
95. Curchod, H.: Rev. méd. de la Suisse Rom. **41**:648 (Oct.) 1921.
96. Hutinel, V., and Merklen, P.: Arch. de méd. d'enf. **24**:521 (Sept.) 1921.

these figures were below the actual, for in those first observed a Wassermann test was not always made. The authors emphasize the fact that, if cases of tuberculous meningitis were studied more carefully as to previous history, clinical, and serologic findings, syphilis would be found more often than it is. There is only one pathognomonic sign of tuberculous meningitis, namely, the presence of tubercle bacilli in the spinal fluid, and these are not easily demonstrated. Because of this difficulty and because of similarity in the two conditions, treatment for syphilis is instituted in all the writers' cases of suspected tuberculous meningitis. If this is not done, there is a possibility of allowing a curable condition to go untreated.

Regan and Cheney[97] observed a case of tuberculous meningitis in a 5-months-old infant, from whom it was impossible to obtain fluid by lumbar puncture. At necropsy this was found to be due to a diffuse infiltration of the pia-arachnoid membrane from the cervical to the lumbar region, with numerous tuberculous granulations which produced marked thickening of the membrane and caused adhesions between it and the dura, almost completely obliterating the subarachnoid space.

Riser and Roques[98] report that in three cases of tuberculous meningitis the preponderance of polymorphonuclear cells in the spinal fluid and the clinical signs of acute meningitis lead to a diagnosis of cerebrospinal meningitis. At necropsy, the meninges showed acute inflammatory changes, although in two of the cases tubercle bacilli were found in the polymorphonuclear cells of the spinal fluid and in the third there was a polyvisceral tuberculosis. The authors believe that the meningeal infection was due to the tuberculotoxins liberated, not on one but on repeated occasions.

Cantilena[99] reports a case of encephalitis with tuberculous meningitis in a 7-year-old child. While in school the child developed a right-sided paralysis without loss of consciousness. The next day there was vomiting, a temperature of 38.6 C. (101.43), and somnolence. Examination showed a convergent strabismus, an up and down movement of the eyeballs, reaction of the pupils to light, but not in accommodation, paresis of the right side of the face and tongue and of the right upper and lower extremity. There was no stiffness of the neck at this time. The cerebrospinal fluid was negative, as was also the blood Wassermann reaction.

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[97] Regan, J. C., and Cheney, G. W. H.: A Case of Tuberculous Meningitis with Dry Spinal Subarachnoid Space Due to Diffuse Tubercle Infiltration of the Spinal Meninges, Am. J. Dis. Child. **22**:516 (Nov.) 1921.

[98] Riser, and Roques: Ann. de méd. **10**:10 (July) 1921.

[99] Cantilena, A.: Riforma med. **37**:458 (May 14) 1921.

On the sixteenth day of illness stiffness of the neck, mydriases, and ptosis developed. The spinal fluid gave a positive Wassermann reaction. Death occurred after forty-six days. Necropsy revealed chronic subacute and acute general miliary tuberculosis. The entire right side of the cerebellum was covered with an area of yellow softening, an encephalitis due to the emboli from the ulcerated gland. Extension of the processes along the cranial nerves and the pyramidal nerve tracts accounted for the paralysis of the eyes and extremities. A later dissemination caused the meningitis and fatal miliary disease.

Slesinger [100] studied an unusual case of abdominal tuberculosis in a 5-months-old baby, who was admitted to the hospital with a diagnosis of probable tuberculous peritonitis. Laparotomy was performed and the abdominal cavity was found to contain intestinal contents and pus from a mesenteric abscess. The child died and necropsy revealed an extensive tuberculous ulceration of the intestines with perforation of one of the ulcers. The mesenteric abscess was in relation to a ruptured tuberculous, caseating gland.

According to Pitts,[101] the belief has been gaining ground that in childhood the intestine may be the primary site of the tuberculous infection, even of the pulmonary type. Pitts reports two cases, one, a miliary tuberculosis in a girl, aged 11 years, and the other, tuberculous meningitis in a 2-year-old boy, in whom a localized tuberculosis of the intestine was apparently the primary lesion. In the first case necropsy revealed in the lower part of the jejunum a number of tubercles, pinhead in size, in and below the mucosa and in the mesentery. Those in the mucosa had not led to ulceration, and the mucous membrane above the tubercles was intact. In the mesenteric, perigastric, and pancreatic lymph glands were tuberculous nodules. In the second case there was a small superficial tuberculous ulcer in the lower part of the jejunum. The mesenteric glands were enlarged and caseous. The cases were of interest not only because the intestine was evidently the portal of entry of the tubercle bacilli, but also because the lesions did not occur in the ileum, where the intestine is richest in lymphoid tissue. The first case showed also that tubercle bacilli can pass into the mucosa without causing superficial injury.

Wrechers [102] had under observation an unusual case of edema, associated with severe intestinal tuberculosis, in a 5-year-old girl. For a few weeks there had been diarrhea and swelling of the ankles and legs. Then the swelling had spread to all parts of the body. On entrance to the hospital the eyes could hardly be opened and examination

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100. Slesinger, E. G.: Brit. M. J. **1**:703 (May 14) 1921.
101. Pitts, H. H.: Canad. M. A. J. **11**:740 (Oct.) 1921.
102. Wrechers, A.: Arch. f. Kinderh. **69**:450, 1921.

of the retina showed swelling of the papillae, more marked on the right side. In both lungs were moist râles; over the left upper lobe fine, crackling râles, and impaired reasonance. The urinalysis and the Pirquet tests were negative. On the eighth day in the hospital the child had a convulsion, followed by difficulty in swallowing and paresis of the left arm. The edema of the left arm and leg was very marked. The diarrhea increased, and the general condition became worse. Death occurred on the sixteenth day. Necropsy showed a solitary tubercle of the cerebellum, hydrocephalus, sinus thrombosis, caseous pneumonia in the left upper lobe, and a few miliary tubercles scattered throughout the lungs, tuberculous pleuritis and peritonitis, and a widespread ulcerative tuberculosis of the small and large intestines.

Frenkel[103] reports two cases of spontaneous gangrene of the extremities in the course of tuberculosis. The first was in a child, aged 2 years, who entered the hospital June 21, 1916, because of edema and cyanosis of the lower extremities which had begun three days before. Examination disclosed that the lower extremities were slightly swollen and of a bluish color, very marked in the toes, which looked as if ink had been poured over them. The discoloration gradually merged into the color of normal skin in the middle of the back of the foot, without any line of demarcation. Pin point hemorrhages occurred in the affected areas. The child was suffering also from pulmonary tuberculosis and hemorrhagic nephritis. The general condition became worse and the child died a month after entrance to the hospital. The second case was that of a boy, aged 5 years. On entrance to the hospital, widespread pulmonary tuberculosis and gangrene of the left leg were observed. Swelling and cyanosis had reached the middle of the calf, but the line of demarcation was at the lower third. The tips of the toes were dry and hard. Death occurred shortly after entrance. At necropsy there was found, besides the widespread tuberculous changes in the lung, a thrombus in the left popliteal artery. Microscopically, the vessel wall showed the picture of a toxic arteritis. The author concludes that obliterative arteritis can be caused by tuberculosis as well as by measles, scarlet fever, diphtheria, pneumonia and other infections. He believes, however, that there must be another factor besides the tuberculous infection or it would be difficult to explain the rarity of this complication of tuberculosis.

Marfan[104] believes that the term "scrofula" should be retained because it represents a pathologic condition occurring in tuberculous individuals. Scrofula is seen, usually, in young children only, and is characterized by chronic cervical adenitis and inflammations of the mucous membrane which tends to ulcerate. A very marked tuberculin test is always present even if there are no demonstrable lesions. The tuberculous lesions in scrofula are characterized by their relative benignity and by their ability to confer a certain degree of resistance to the individual.

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[103] Frenkel, H.: Ztschr. f. Kinderh. **29:**213 (June) 1921.

[104] Marfan, A. B.: Paris méd. **34:**13, 1921.

Ernberg[105] reviews eighty-six cases of erythema nodosum in children and is convinced that this is a manifestation of an anaphylactic process in the course of tuberculosis. He found that the lesions appear in a comparatively early stage of tuberculosis, accompanied by fever, pain in the joints, sometimes marked pallor, pain in the abdomen, and albuminuria. The tuberculous lesions were usually in the bronchial glands and were discovered only by roentgen ray. When the erythema appeared during a late stage, there occurred, in a number of cases, pulmonary symptoms, due evidently to an acute process in the glands. But in nearly all instances, manifestations of active tuberculosis developed after the erythema had run its course. Sometimes this was a generalized tuberculosis. As a rule, all the children reacted positively to tuberculin, even the younger ones, in whom a positive reaction is not the rule.

That the erythema nodosum is an anaphylactic process was shown by the histologic examination of the lesion which was similar to the one produced by the infection of tuberculosis, by the general and local reaction which accompanies the appearance of the eruption, and by the similarity of the entire process to other well known anaphylactic reactions.

Dietl[106] describes a case of tuberculosis of the skin in an infant, aged 19 months, due to infection of an impetigo lesion with tubercle bacilli. When the child was brought for examination, there were typical lesions of impetigo on the dorsum of each foot. On the back was an oval ulcer, 1.5 by 2 cm., partly covered by a scab with the edges infiltrated. The glands in the axilla were the size of a hen's egg; the lungs were normal. The Pirquet test, which had been negative eight weeks before, was now strongly positive. Three months later the child had developed phlyctenular conjunctivitis. The impetigo on the feet had disappeared but the ulcer on the back was still present. It was excised and on microscopic examination proved to be tuberculous. The author believes that the child contracted impetigo and infected the lesion by rubbing tuberculous material into it.

Stillians[107] reports a case of tuberculosis verrucosa cutis, associated with lupus vulgaris and lichen scrofulosorum in a boy, aged 10 years. On the back of the four small toes of the left foot was a warty tumor,

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105. Ernberg, H.: Jahrb. f. Kinderh. **95**:1, 1921.
106. Dietl, K.: Monatschr. f. Kinderh. **22**:27 (Oct.) 1921.
107. Stillians, A. W.: Internat. Clin. **2**:32, 1921.

1½ inches (4 cm.) in length and breadth, and ¼ (6 mm.) inch in height, covered with papillary projections; some dark brownish red, others covered with thick, horny, light brown crusts. On the external, anterior surface of the left instep was a second lesion, in part like the one on the toes and partly covered with a thin crust, on removing which a brownish-red erosion remained. Just above the ankle on the external and posterior surface of the leg was a brownish-red, weeping erosion, 3 inches (7.6 cm.) in diameter. Above this was a little larger patch of similar nature. The patient was treated with roentgen ray and soon after a papular eruption appeared, first on the chest, then on the abdomen, arms, and upper thighs. These papules became acuminate and capped by a tiny scale. They were dull red, from $\frac{1}{16}$ to ⅛ inch (from 1.5 to 3 mm.) in diameter. The author believes that, without doubt, he was dealing with a group of tuberculous skin lesions; tuberculosis verrucosa cutis on the feet, a superficial type of lupus vulgaris on the leg, and lichen scrofulosorum on the chest, abdomen and arms.

Low[108] describes the various forms of tuberculosis of the skin. Of all these the one which most concerns the general practitioner is lupus vulgaris, when it occurs in multiple lesions. Numerous small red spots suddenly appear scattered over the face, body, and limbs, which show on pressure the apple-jelly like nodules of tuberculosis. This form is found more often in children and adolescents, and often follows one of the exanthems, especially measles. It is embolic in origin and is an evidence of an active tuberculosis somewhere in the body. Another group of tuberculous skin lesions, which are very important, are the tuberculids, namely, lichen scrofulosorum, papulonecrotic tuberculids, sarcoids, and erythema induratum. Lichen scrofulosorum appears in small papules often on the sides of the chest. The papules are arranged in groups; at first pink, surmounted by a minute scale, and in a few weeks becoming brown. If the eruption is very acute, there may be small vesicles or pustules, instead of papules.

The papulonecrotic tuberculid consists of slightly larger lesions than lichen scrofulosorum. These appear as bluish-red papules, the centers of which undergo first a process of necrosis, then crust over, and slowly heal. Crops of eruption appear from time to time.

Erythema induratum scrofulosorum is the best known of the tuberculids. It occurs as rounded or oval bluish-red swellings, frequently on the lower part of the back of the legs. If these swellings break down and ulcerate, their appearance is similar to broken down gummas. After healing, a scar remains, often surrounded by a pigmented area. Another tuberculid is that described by Broch as a sarcoid. It is found as single or multiple hemispherical purple elevations of the skin, and usually located on the face or upper extremities.

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[108] Low, R. C.: Edinburgh M. J. **29**:114, 1920.

The treatment of these forms of tuberculosis of the skin is not altogether satisfactory. With rest and general treatment, as for all forms of tuberculosis, most of them, especially the small lesions, disappear. For the larger lesions, such as erythema induratum, the roentgen rays are useful.

DIAGNOSIS

Güterboch[109] is certain that with increasing age, the number of children infected with tuberculosis grows, so that at the age of puberty about one-half are tuberculous. In most instances, infection takes place after birth, but intra-uterine acquired tuberculosis is more common than is usually supposed, because women with a latent tuberculosis can suffer from placental tuberculosis and infect the fetus. The author's experience coincides with that of other writers who find the younger children of the family more frequently the victims than the older. Hilum involvement seems to be the most common form of tuberculosis in children. When the process extends beyond the hilum into the pulmonary parenchyma, the outcome is usually fatal. Apical involvement, however, is not uncommon in children over 5 years of age. The disease apparently runs a similar course in members of the same family, even when there is no family history of the disease.

Pollitzer[110] always found a tuberculous process in the lungs or hilum glands with the roentgen ray in nonrachitic children who had a positive Chvostek's sign. The sagittal thoracic diameter was greater than normal in 70 per cent. of such children, whereas in rachitic children with a positive Chvostek sign the transverse diameter of the chest was greater than normal in 60 per cent. of the cases. He found also that in tuberculous children with a positive Chvostek sign the distance from jugulum to the symphysis pubis was shorter than normal in 60 per cent. of the cases. Pollitzer believes that demineralization which is common in tuberculosis may be responsible for the over-excitability of the nerves causing Chvostek's sign.

Comby[111] is of the opinion that the so-called "typhobacillose" of Landouzy is only a form of tuberculosis with the tuberculous lesion latent. It is an error to believe that there can be fever of tuberculous origin without a lesion somewhere in the body. In children, this lesion is usually in the bronchial glands and ought to be found by auscultation, by roentgen ray, or by the fluoroscope.

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[109] Güterboch, R.: Beitr. z. Klin. d. Tuberk. **43**:297, 1920.

[110] Pollitzer, R.: Policlinico **28**:1067 (Aug. 8) 1921.

[111] Comby, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:939 (June 24) 1921.

Tronconi[112] believes that Zinda's sign is a very important aid in the diagnosis of tuberculous meningitis. This sign consists of a sudden raising and jerking forward of the shoulders when the head is passively moved to the other side. The shoulder remains in this position and resists all efforts to bring it back until the head is again turned toward the median line. Tronconi never found the sign in healthy children or in children suffering from any disease except tuberculous meningitis. He was, on the other hand, able to obtain it in all children with tuberculous meningitis and in every instance he found the diagnosis confirmed at necropsy.

Richard[113] is of the opinion that children of tuberculous parents are born with attributes which make them an easy prey for the disease. This is true also of children with lymphatic diathesis. To make a diagnosis of a pretuberculous child, it is necessary to take a careful history, including that of frequent coughs and colds. Next in importance is the general examination of the child.

Stewart[114] discusses the value of the various diagnostic methods in pulmonary tuberculosis among children. He bases his conclusions on the study of 300 children between 5 and 14 years of age, and thinks that family and personal history lead but a little way toward a diagnosis. Laboratory investigation is limited to the few instances in which the sputum is available. Physical examination is very valuable, but its results are sometimes indefinite in regard both to the existence of active disease and often to the true nature of the morbid changes found. Of the specific tests the quantitative cutaneous is of the greatest value. Radioscopic examinations are unsatisfactory. No one method, then, except the finding of tubercle bacilli in the sputum, can be depended on to make a final diagnosis of tuberculosis in children; but two methods combined, namely, physical examination associated with the quantitative cutaneous test, are preeminently reliable.

O'Brien and Ames[115] have made a study of the roentgen ray and tuberculosis in children. According to these writers it is commonly accepted that the roentgen ray usually shows structural changes of much greater extent than physical examination would suggest. It has been noted also that the roentgenogram is positive in many cases in which the physical examination is negative. These findings were corroborated in the authors' series of forty-four cases. Fifteen cases were given a negative diagnosis by clinical examination, yet showed structural lung changes consistent with pulmonary tuberculosis. Because of these

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112. Tronconi, S.: Pediatria **29**:802 (Sept. 1) 1921.

113. Richard, P.: Arch. de méd. d'enf. **24**:215 (April) 1921.

114. Stewart, S. H.: Tubercle **2**:193 (Feb.) 1921.

115. O'Brien, F. W., and Ames, F. B.: Roentgen Ray and Tuberculosis in Infants and Children, J. A. M. A. **76**:1474 (May 28) 1921.

findings, the authors advocate the more routine use of the roentgen ray, in a way analogous to the tuberculin skin tests.

Méry, Détré and Desmoulins [116] emphasize the importance of confirming a clinical diagnosis of tuberculosis in childhood by roentgen-ray examination. Three stages of hilum tuberculosis are recognized. In the first stage the shadows extend hardly beyond one or two intercostal spaces, and the right shadow is more apparent than the left. These shadows are not diagnostic of tuberculosis but are a manifestation of any respiratory disease. In the second stage the shadows are hazy, and spread out each side of the median shadow like the wings of a butterfly; at times the shadow is unilateral. These shadows indicate an active tuberculosis. In the third stage the shadows of the hilum are clear cut, the ramifications are dark and reinforced by small calcifications, either in groups or scattered; the shadows are more extensive and may reach as high as the clavicle or as low as the diaphragm. Sometimes there are present isolated shadows at the bases, in the lateral portions, or in fact anywhere in the lungs, and those, according to the writers, are of significance and probably represent the primary infection of the tracheobronchial adenopathy.

In order to determine the importance of certain physical signs and roentgen-ray findings as indicators of the degree of infection in the tracheobronchial glands, Balyeat [117] examined 449 children under 16 years of age. Especial significance was placed on D'Espine's sign as an indicator of tracheobronchial adenopathy and the appearance of hilum shadows in the roentgenogram as a means of differentiating tuberculous from nontuberculous glands. Balyeat considers D'Espine's sign positive if the tracheal voice is heard below the seventh cervical vertebra in children under 3 years of age; below the first dorsal in children between 3 and 5 years of age; or below the third dorsal in children over 5 years of age. In 116 of the 449 children there was a positive D'Espine's sign. Practically all patients on whom was elicited a positive D'Espine's sign or from whom a history of contact was obtained were roentgenographed. The author believes that only by means of roentgenograms can a tuberculous hilum be differentiated from one that is nontuberculous.

Dunn and Cohen,[118] discussing the diagnosis and the prognosis of tuberculosis in infancy, base their conclusions on a series of 374 cases, in which a clinical diagnosis of tuberculosis was made, and on a series of 138 necropsies, in which lesions of tuberculosis were found. They believe that special methods of diagnosis are needed for the recognition of the primary focus in the lung, and adopt the following routine measures: The lungs are examined not only for signs of consolidations but also for signs of enlargement of the tracheobronchial lymph nodes. The signs especially looked for are interscapular dulness, prolongation downward of the normal cervical dulness, and D'Espine's sign. The Pirquet cutaneous reaction is made and repeated at intervals, and in suspicious cases a roentgenogram of the chest is taken. If the Pirquet reaction is positive or even suspicious, or if the roentgenograms show the shadow characteristic of tracheobronchial node enlargement, a diagnosis of tuberculosis, primary in the lung, may be made with a fair degree of certainty. If the sole evidence is a positive D'Espine's sign of interscapular dulness, the diagnosis may be made with only a slight degree of probability. In cases in which all three of these forms of evidence are absent, tuberculosis in the primary stage should not be diagnosed. The secondary stage, except in cases of tuberculous bronchopneumonia and general miliary tuberculosis, offers no difficulty in diagnosis. In the majority of cases showing pulmonary consolidation, in which either the Pirquet reaction or the roentgen-ray plate is positive, the correct diagnosis is tuberculous bronchopneumonia.

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[116] Méry, H.; Détré, G., and Desmoulins, A.: Presse méd. **29**:221 (March 19) 1921.

[117] Balyeat, R. M.: Diagnosis and Significance of Tracheobronchial Adenopathy, J. A. M. A. **76**:988 (April 9) 1921.

[118] Dunn, C. H., and Cohen, S. A.: The Diagnosis and Prognosis of Tuberculosis in Infancy, Am. J. Dis. Child. **21**:187 (Feb.) 1921.

Debré [119] takes the position that we should always suspect tuberculosis in an infant if another member of the family has it; in fact, many go so far as to consider these infants as positively having tuberculosis. The tuberculin test is of great help when positive, but if negative it should be repeated after several months, for it must be remembered that it takes several months for the organism to develop susceptibility to tuberculin.

Vienna is a city in which tuberculosis has always been widespread, and the war conditions there made it possible for Pirquet [120] to study the pathogenesis and the control of that disease even more closely than before. He states that infection with the tubercle bacillus is pulmonary in 90 per cent. of all cases, and is called "bronchogenetic." The "enterogenetic" form, affecting the intestines, is not so common where milk is usually boiled, but is found more often in countries like the United States and England, where this is not done. The "stomatogenetic" and the "dermatogenetic" forms are very unusual, and one almost never sees the "placentogenetic" form, for the infant usually dies very soon after birth. Tuberculosis, like syphilis, has a primary, secondary, and a tertiary stage. The older and stronger a child, the better it can, while in the first stage, develop a resistance which consists either of greater sensibility or greater immunity, depending on the kind of anti-

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119. Debré, R.: Médecine **2**:626 (May) 1921.
120. Pirquet, C.: Policlinico **28**:551, 1921.

bodies formed. The less the child's organism can accomplish this, the sooner it enters the second stage, the dissemination of the germs to all parts of the body. Toward the end of childhood, there appears a development that seems to have some connection with puberty and takes the form of a cavernous destruction of the apex of the lungs. This has been called the third stage, although it may be more a tendency of the tissues, due to the age of the subject, than a true development of the disease.

PROGNOSIS

Debré, Paraf and Dautrebande[121] believe that the prognosis of tuberculosis in infants can be determined by the length of time between infection and the appearance of a positive tuberculin reaction, namely, the antiallergic period. This can usually be ascertained by a series of cutaneous tests at regular intervals, begun as soon as it is known an infant has come in contact with a tuberculous person. Clinical facts and animal experimentation have shown that infection with massive doses of tubercle bacilli causes a short antiallergic period, whereas small doses produce a long antiallergic period. A short antiallergic period, therefore, always means a massive infection, which is followed by a fatal tuberculosis, and a long antiallergic period signifies an infection with few bacilli and a benign course.

Nobel[122] reports his conclusions with regard to the prognosis of pleuritis in childhood. In all, seventy-eight children were observed, and in the entire series tuberculosis was the only etiologic factor found. Thirteen of the children died, twenty-six could not be reexamined after they had left the hospital, and thirty-nine were kept under observation from a period of a few months to nineteen years. In 41.1 per cent. of these, recovery was complete, in 38.4 per cent. there were only slight changes on physical and roentgenologic examination referable to the previous pleurisy, in 10.2 per cent. there were more or less severe changes, such as retraction of the affected side, displacement of the heart, scoliosis, and marked pulmonary infiltration. Therefore, he believes that the prognosis of tuberculous pleurisy is quite favorable.

Harbitz[123] cites cases of tuberculous meningitis which have ended in recovery, and reports necropsies in which healed tubercles have been found. From his observations, Harbitz concludes that tuberculous meningitis may heal, even when there are extensive lesions with exudate and tubercle formation. This curable form occurs largely in persons who have suffered from chronic and relatively benign forms of

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121. Debré, R.; Paraf, J., and Dautrebande, L.: Ann. de méd. **9**:443 (June) 1921.

122. Nobel, E.: Wien. klin. Wchnschr. **34**:423 (Sept. 1) 1921.

123. Harbitz, F.: Am. J. M. Sc. **161**:212 (Feb.) 1921.

tuberculosis. It is probable, however, that a more important factor is the resistance of the body which increases with the age of the patient. This is borne out by the fact that, whereas about 60 per cent. of all cases of tuberculous meningitis occur in the first two years of life and quite regularly result in death, recovery has occurred among older children and adults.

Debré and Bernard[124] report a case of tuberculosis in an infant which illustrates the fact that the disease is not invariably fatal at this time of life, and that a long antiallergic period means a benign course. The child was removed from the tuberculous mother on the forty-ninth day of life, and did not give a positive cutaneous reaction until 2½ months old. At that time there were also clinical evidences of infection. Roentgen-ray examination revealed a shadow in the sixth interspace on the right side. In two or three weeks all symptoms subsided and only a latent tuberculosis remained, as revealed by the roentgen ray and positive tuberculin reaction.

TREATMENT

Broca[125] calls attention to the favorable influence of the roentgen ray on tuberculous adenitis. He is very conservative in regard to the total extirpation of the glands. Nevertheless, he finds it valuable in the hands of experienced surgeons in cases of fistulas, which have resisted heliotherapy and roentgen-ray treatment.

D'Oelsnitz and Carcopino[126] report a case of tracheobronchial adenopathy causing symptoms of suffocation, which was successfully treated by roentgen ray. The patient was a 3-year-old child, who suddenly awakened one night with a cry of suffocation. On entrance to the hospital there was slight cyanosis, dyspnea and substernal retraction. The respiratory murmur was diminished on the right side. Roentgen-ray examination showed shadows of enlarged hilum glands, especially on the right side. Immediate amelioration of the dyspnea and retraction of the chest followed treatment with the roentgen ray. From the study of this and other cases the writers believe that a severe congestion of inflammatory reaction in the tuberculous glands caused the symptoms of suffocation and on these reactions the roentgen ray has a very rapid action. They are also of the opinion that the roentgen ray can cause retrogression of chronically enlarged mediastinal glands and can prevent these acute exacerbations. While preparing this article, the authors had occasion to observe a similar case in a 2-year-old child, whose condition also yielded to roentgen-ray therapy.

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124. Debré, R., and Bernard, L.: Bull. et mém. Soc. méd. d. hôp. de Paris **44:**1658 (Dec. 31) 1921.

125. Broca, A.: Progrès. méd. **36:**227 (May 21) 1921.

126. D'Oelsnitz, M., and Carcopino, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **45:**297 (March 4) 1921.

Hubeny[127] states that in recent years the more general application of the roentgen ray for tuberculous adenitis has proved its worth beyond a doubt. The results obtained by roentgen-ray therapy are so uniformly good that it can be safely recommended as the most useful method of treatment. The roentgen ray, in producing healing of tuberculous glands, causes actual destruction of the tuberculous granulation tissue.

Boggs[128] has found in the treatment of tuberculous adenitis that better results are obtained from the use of radium and roentgen ray than from any other method. Radiotherapy alone will cure over 90 per cent. of the cases. Surgeons of experience do not operate primarily for tuberculous adenitis. If they operate, it is only to remove fibrous nodes, after the tuberculous foci have been destroyed by the roentgen ray.

Mulier[129] treated thirty cases of glandular tuberculosis, fourteen of pleuritis, and twenty-two of exudative and adhesive peritonitis with rays from the quartz lamp. The favorable effect was first noticed in the general condition, then followed improvement of the tuberculous focus. Usually from forty to fifty treatments were necessary before complete cure was effective.

Oldenburg[130] publishes the results of sanatorium treatment of 120 children under 4 years of age with pulmonary tuberculosis. Of thirty-seven children below 2 years twenty-five were cured, two improved, and ten died. Of eighty-three children between 2 and 4 years of age, thirty-seven were cured, thirty-one improved, five did not improve, two became worse, and eight died. Later results were studied in 105 children, 64 per cent. remained well six years, 20 per cent. died within the six years, and no information could be obtained regarding the remaining 16 per cent.

Achard[131] does not agree with the general opinion that latent tuberculosis in childhood requires only hygienic, dietetic, and climatic treatment. These must not be neglected but often the administration of tonics is indicated. Iron, arsenic, and manganese are the best drugs to increase the amount of hemoglobin and the number of red blood cells. Beside a suitable diet, it is well to supply an excess of fat, the best form of which is cod liver oil. He feels that children who have been infected with the tubercle bacillus require specific immunization. Old tuberculin is not very satisfactory, since it does not contain all the reactive corpuscular substances of the tubercle bacillus, but there are three preparations which are very satisfactory, Much's partial antigens,

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127. Hubeny, M. J.: Internat Clin. **1**:110, 1921.
128. Boggs, R. H.: Am. J. M. Sc. **162**:90 (July) 1921.
129. Mulier, A.: Pedjatria Polska **1**:2, 1921.
130. Oldenburg, T.: Ugesk. f. Laeger. **83**:683 (May 26) 1921.
131. Achard, H. J.: Am. Rev. Tuberc. **5**:405 (July) 1921.

von Ruck's vaccine, and Crofton's (Dublin) antigen. These preparations can bring about complete immunization. Achard believes that deliberate and extensive immunization against the tubercle bacilli would go far toward reducing the morbidity of tuberculosis among adolescents and adults, in ten, twenty or thirty years from now.

After six and a half years of experience, Hyde and Grasse[132] are convinced that much better results can be obtained in cases of surgical tuberculosis, if the disease is not regarded as purely surgical. This type of the disease is a general constitutional one with local manifestation. The authors combine surgery with heliotherapy. Favorable progress is in direct proportion to the intensity of the pigmentation. The most striking local result in the treatment of joint tuberculosis by heliotherapy, and one of greatest importance in early cases, is the preservation of motion in the affected joints. The sun acts as an agent of repair on bone tissue. The effect on sinuses and ulcers is one of marked reaction, and on lymph nodes a reduction in size and absorption of broken down tissue. The effect on effusion in joints, peritoneal and pleural cavities is one of absorption.

The method of alimentary therapy developed by Pirquet[133] has given excellent results after the failure of every medical form of treatment including tuberculin therapy. His theory is that the formation of antituberculosis antibodies is related to a rich metabolism, and that the whole value of climate in the treatment of tuberculosis lies in finding a climate that excites the patient's appetite and in satisfying it. The nutritional prescription is made out according to the "Nem" system. When no restrictions are necessary, the diet is very simple. Meat is given once a week, the rest of the time milk, starches, potatoes, green vegetables, and fats, a diet easily combined with that of a family. This method of treatment has given excellent results with 100 children under observation; every other form of therapy was gradually abandoned.

König[134] warns against trusting too blindly to conservative treatment of bone, joint, and glandular tuberculous processes outside of well equipped institutions, saying that the results reported by Bier are experimental, as the ultimate outcome is not yet known. König has investigated 1,932 resections reported from twenty sources, five, ten, twenty, or more years ago, and has found that although these were the gravest kinds of tuberculous processes, 68 per cent. have been permanently cured to date.

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132. Hyde, C. L., and Grasse, H.: Am. Rev. Tuberc. **5**:159 (April) 1921.

133. Pirquet, C.: Policlinico **28**:551, 1921.

134. König, F.: München. med. Wchnschr. **68**:642 (May 27) 1921.

Harms[135] reports his experience with artificial pneumothorax in the treatment of tuberculosis of childhood. He has used this method with thirty-seven children, two in the second stage of hilum tuberculosis, and thirty-five in the third. In seven it was impossible to fill the pleura because of adhesions. Five of the children were cured after from twelve to forty-eight months' treatment, four died during treatment, and eleven after the course of treatment was finished. Two children were still under treatment at the time of his report and eight had passed from observation. Harms thinks the treatment should not be undertaken with children under 18 months of age. The technic is the same as that used in adults.

Cole[136] details the surgical treatment of tuberculosis in children.

Homuth[137] had in his care a child in whom an acute ileus was the first symptom of mesenteric tuberculosis. The patient was a 13-year-old school girl who had never had any gastro-intestinal disturbance. Three days before admission to the hospital she developed symptoms of intestinal obstruction with vomiting. When admitted, the child was pulseless, the abdomen being markedly distended, and there was constant vomiting. Operation was immediately performed and the mesentery was found firmly adherent to the intestine. In the mesentery were large, cheesy, tuberculous glands. As it was impossible to free the adhesions, a resection was performed and the patient recovered.

Lefert[138] emphasized the danger of removing the fluid in cases of ascitic tuberculous peritonitis. The exudate contains antibodies needed to combat the disease. If the fluid is removed by puncture, it should be reinjected subcutaneously.

The fact that local surgical tuberculous lesions are metastatic in origin lead Klare[139] to look for pulmonary lesions with the roentgen ray in children suffering from surgical tuberculosis. In most instances pulmonary and bronchial gland lesions were found, and the author emphasizes the importance of treating surgical tuberculosis as a general disease and not limiting it to the local condition.

In discussing the surgical aspects of abdominal tuberculosis, Ladd[140] says that the variety of types of manifestations has led to confusion in its treatment, but there is sufficient data at hand to warrant the establishment of more uniformity of management than at present exists. First in importance should be placed proper hygiene, diet, and outdoor life. Surgery as an aid in selected cases is of unquestionable value, but the

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135. Harms: Aerztl. Rundschau, München. **30**:333, 1920.
136. Cole, W. H.: Minnesota Med. **4**:228 (April) 1921.
137. Homuth, O.: Deutsch. med. Wchnschr. **47**:777 (July 7) 1921.
138. Lefert, M. V.: Arch. Espan. de Pediatria **5**:449, 1921.
139. Klare, K.: Beitr. z. Klin. de Tuberk. **46**:183, 1921.
140. Ladd, W. E.: Boston M. & S. J. **185**:317 (Sept. 15) 1921.

cases should be logically chosen as far as difficulties of diagnosis make it possible. If the diagnosis can be made in the stage of localized mesenteric adenitis, excision of the glands is logical, successful, and probably prevents the development of the other stages. If caseous glands are found on operation, when an erroneous diagnosis of appendicitis has been made, they should be removed. If a large single mesenteric abscess is found, it should be incised, the pus evacuated, the cavity wiped out with iodin, and the abdomen closed without drainage. In the ascitic stage laparotomy with evacuation of the fluid is recommended when the patient fails to respond to medical treatment after a reasonable length of time. In the plastic stage, the prognosis is poor with any treatment and operation is resorted to only to relieve the intestinal obstruction, and in this it has occasionally been successful.

Mixter[141] also discusses the surgical aspect of abdominal tuberculosis in children. He believes the indication for operation in tuberculous mesenteric adenitis is clearly defined. There is a localized process which is potentially capable of causing a disseminated peritoneal infection or an acute miliary process. As elsewhere, it should be removed if possible. Operation should be advised in the ascitic form only when improvement does not take place after a fair trial of medical treatment, and when an active process elsewhere can be ruled out. For the last seven years Mixter has been introducing from 300 to 1,200 cm. of air after withdrawal of the fluid. Nineteen of forty-nine cases were treated in this way, and the results suggest that air injection may give more beneficial results than simple laparotomy. In treatment of the plastic type, operation is of no value save in meeting complications and emergencies as they arise. Hygienic treatment is of paramount importance. Surgery should only aid and never supplant it.

Brauer,[142] in discussing the surgical treatment of pulmonary tuberculosis in children, says the only procedure to be considered is artificial pneumothorax. The tendency of the disease to become generalized, the preponderance of hilum lesions, and of hepatization must be borne in mind, when the disease is considered in connection with children. Hepatization does not respond well to this method of treatment, and only when the hilum process has spread to involve extensive areas of the lung is there any prospect of benefit.

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141. Mixter, C. G.: Boston M. & S. J. **185**:557 (Nov. 10) 1921.

142. Brauer, L.: Ztschr. f. Tuberk. u. Heilstättenw. **34**:647 (Oct.) 1921.

American Journal of Diseases of Children

VOL. 27 MAY, 1924 No. 5

THE PRODUCTION OF PURULENT MENINGITIS IN THE RABBIT AND THE CHANGES IN ITS CEREBROSPINAL FLUID *

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Purulent meningitis in animals has been studied in recent years by many observers, among whom may be mentioned Ritchie,[1] Wollstein,[2] M'Donald,[3] Councilman, Mallory and Wright,[4] Von Lingelsheim,[5] and Flexner.[6]

Ritchie produced purulent meningitis in the monkey by the intraspinal injection of *B. influenzae*. Similar results have been described by Wollstein. Councilman, Mallory and Wright succeeded in producing meningitis in the goat by the injection of the meningococcus into the spinal canal. Von Lingelsheim introduced the meningococcus intraspinally into two monkeys. The animals developed rigidity of the neck and of the dorsal muscles, and had a violent attack of vomiting. Similar results have been obtained by Flexner and M'Donald; other observers have, however, obtained negative results.

In the first paper I stated that the injection of virulent tubercle bacilli into the subarachnoid space of rabbits causes tuberculous meningitis, characterized by an incubation period of from five to fifteen days, followed by a period of cerebral symptoms ending almost invariably in death.

The object of this investigation is to study the changes in the spinal fluid of the rabbit in which purulent meningitis, due to pyogenic organ-

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* Received for publication, Dec. 17, 1923.

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1. Ritchie, J.: J. Path. & Bacteriol. **14**:615, 1910.
2. Wollstein: J. Exper. Med. **14**:73, 1913.
3. M'Donald, S.: J. Path. & Bacteriol. **12**:442, 1908.
4. Councilman, Mallory and Wright: Report of State Board of Health, Boston, 1898.
5. Von Lingelsheim: Deutsch. med. Wchnschr. **31**:1217, 1905.
6. Flexner, S.: J. Exper. Med. **9**:142, 1907.

isms, has been produced experimentally. Adult rabbits were used in all the experiments. The micro-organisms which we employed for these experiments were pneumococcus, *B. coli, B. inflenzae, B. pyocyaneus,* streptococci and staphylococci.

The inoculation materials were emulsified in 0.65 per cent. salt solution. The inoculation was made by an intraspinal injection. It was effected through the posterior occipito-atloid ligament. The quantity of bacterial suspension varied from 0.25 to 0.3 c.c. The spinal fluid was withdrawn to an extent somewhat larger than the amount of suspension to be injected. The injection was made extremely slowly.

Without entering on the details of the experiments, I may make the following general statement: The inoculation of the before mentioned pyogenic organisms into the subdural space of the rabbit produces a disease characterized by a latent period of from several hours to three days, depending on the dosage and virulence of the injected organisms, followed by a period of ataxia and paralysis. From the time of the appearance of the first symptom, the severity rapidly increases and death occurs in from two to five days or somewhat later. The cerebrospinal fluid is, without exception, opaque or purulent, containing numerous polymorphonuclear leukocytes. It sometimes deposits purulent sediment. The organisms are present and demonstrable by culture and by film preparation. By necropsy it may be ascertained that certain changes are common to all the forms of meningitis. It shows purulent leptomeningitis, both on the surface of the brain and within the sulci, as well as over the spinal cord. Microscopically, it shows an extensive exudation in the pia. This consists chiefly of polymorphonuclear leukocytes. In some cases hemorrhages are found in the meninges.

There is no visible change in the abdominal and thoracic viscera. We have examined the cerebrospinal fluid at varying periods after the intraspinal inoculation with the before mentioned pyogenic organisms.

EXPERIMENT WITH PNEUMOCOCCI

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of the pneumococci. One culture on blood agar is suspended in 4 c.c. of 0.65 per cent. saline solution. A few hours after inoculation the first cerebral symptom begins. Definite paralysis occurs on the second or third day. Death occurs from the third to the fifth day. Necropsy shows fibrinous inflammatory exudation in the pia, attended by hyperemia, infiltration with polymorphonuclear leukocytes. No gross changes are visible in other organs. The results are shown in Table 1.

TABLE 1.—*Experiments with Pneumococci*

							Cells per C. Mm.		
Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Polymorphonuclear	Lymphocyte	Remarks
1	1st	Cloudy turbid	+	0.033	0.034	+	240	46	Leptomeningitis
2	2d	Turbid	Gelatinous character	0.060	0.025	++	350	20	Leptomeningitis
3	4th	Cloudy turbid	Gelatinous character	0.060	0.031	++	950	53	Leptomeningitis
4	5th	Turbid	+	0.096	0.034	++	1,099	103	Leptomeningitis
5	5th	Cloudy turbid	Gelatinous character	0.126	0.02	++	1,238	93	Leptomeningitis

EXPERIMENT WITH COLON BACILLI

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of colon bacilli. It was isolated from the stool of an infant suffering from accute enteritis. (The subcutaneous injection with 0.1 mg. of the culture causes a small pustule to form in a mouse after twenty-four hours.) The first cerebral symptom begins two or three hours after inoculation and death occurs within a few days. Necropsy shows that the pia is hyperemic. Opacity and thickening of the membrane are seen. Microscopical examination shows an exudate of abundant leukocytes. No gross changes are seen in other organs. The results are shown in Table 2.

TABLE 2.—*Experiments with Colon Bacilli*

							Cells per C. Mm.		
Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Polymorphonuclear	Lymphocyte	Remarks
1	1st	Cloudy turbid	+	0.105	0.025	++	2,860	510	Leptomeningitis
2	1st	Turbid	+	0.264	0.019	++	2,960	81	Leptomeningitis
3	2d	Cloudy turbid	+	0.305	0.028	++	3,058	196	Leptomeningitis
4	2d	Cloudy turbid	Gelatinous character	0.26	0.009	++	2,861	103	Leptomeningitis
5	2d	Turbid	Gelatinous character	0.196	0.01	++	3,412	201	Leptomeningitis

EXPERIMENT WITH B. PYOCYANEUS

The rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *B. pyocyaneus.* (The intradermal inoculation with 0.1 c.c. of this suspension causes an abscess of 6 mm. in size to form in a guinea-pig after twenty-four hours.) After intraspinal injection, a disease is developed in the animal, characterized by a latent period of from four to five hours, followed by a period of cerebral symptoms that terminates in death within three days. On necropsy, the meninges of the brain and spinal cord are seen to be inflamed and often covered with a purulent exudation, which is most marked at the convexity of the brain. No visible changes are seen in the abdominal and thoracic viscera. The results are given in Table 3.

Table 3.—*Experiments with B. Pyocyaneus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.048	0.031	++	2,860	280	Leptomeningitis
2	2d	Cloudy turbid	+	0.024	0.026	+	680	171	Leptomeningitis
3	2d	Turbid	+	0.056	0.035	++	563	240	Leptomeningitis
4	2d	Cloudy turbid	+	0.096	0.019	++	1,238	192	Leptomeningitis
5	3d	Turbid	+	0.16	0.034	+	907	121	Leptomeningitis
6	3d	Cloudy turbid	+	0.098	0.038	+	708	201	Leptomeningitis

EXPERIMENT WITH STREPTOCOCCI

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of streptococci. (The intradermal inoculation with 0.1 c.c. of this suspension causes a local abscess of 5 mm. in size to form in a rabbit after twenty-four hours.) The animal in the incubation period of from two to three days is apparently normal. Definite paralysis occurs on the fourth day. The disease terminates in death. The pia mater is everywhere congested and appears hazy and opaque. A fibrinous inflammatory exudation is seen in the meninges. This consists chiefly of polymorphonuclear leukocytes. The abdominal and thoracic viscera are negative. The results are shown in Table 4.

Table 4.—*Experiments with Streptococci*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Remarks
							Polymorphonuclear	Lymphocyte	
1	1st	Turbid	+	0.13	0.022	+	1,034	204	Leptomeningitis
2	1st	Cloudy turbid	+	0.086	0.009	+	2,085	455	Leptomeningitis
3	2d	Turbid	+	0.26	0.03	+	963	204	Leptomeningitis
4	2d	Turbid	++	0.18	0.032	++	1,077	104	Leptomeningitis
5	2d	Cloudy turbid	+	0.09	0.01	++	2,060	107	Leptomeningitis
6	3d	Turbid	+	0.13	0.009	+	1,963	203	Leptomeningitis
7	4th	Cloudy turbid	+	0.10	0.022	+	673	209	Leptomeningitis
8	6th	Turbid	+	0.09	0.020	+	870	120	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS AUREUS

Rabbits are injected intraspinally with 0.3 c.c. of suspension of *Staphylococcus aureus*. (The intradermal inoculation with 0.1 c.c. of this suspension causes a pustule 3 mm. in size to form in a rabbit after twenty-four hours.) A few hours after the intraspinal inoculation the animal becomes ataxic. On the second day paralysis of the legs occurs. Death is on the fourth or fifth day. Necropsy shows traces of fibrinous exudate over the whole base, and extending upward on the convex surface of the brain and the cerebellum. Frequently the posterior half of the brain is covered with a thick layer of pus. There are no visible changes in other organs. The results are given in Table 5.

TABLE 5.—*Experiments with Staphylococcus aureus*

							Cells per C. Mm.		
Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Polymorphonuclear	Lymphocyte	Remarks
1	1st	Turbid	+	0.123	0.041	++	1,036	441	Leptomeningitis
2	2d	Cloudy turbid	+	0.095	0.035	++	1,024	763	Leptomeningitis
3	4th	Cloudy turbid	Gelatinous character	0.230	0.03	++	1,930	410	Leptomeningitis
4	4th	Cloudy turbid	+	0.123	0.026	++	1,980	120	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS ALBUS

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *Staphylococcus albus.* (The intradermal injection with 0.1 c.c. of this suspension causes an abscess 2 mm. in diameter to form in a rabbit after twenty-four hours.) A few hours later, the animal becomes excitable, ataxic, and paralytic. Death occurs within a few days. On necropsy it is found that there are extreme congestion, thickening and matting of the pia mater. There is no gross change in the other organs. The results are given in Table 6.

TABLE 6.—*Experiments with Staphylococcus albus*

							Cells per C. Mm.		
Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Polymorphonuclear	Lymphocyte	Remarks
1	1st	Turbid	+	0.065	0.048	++	245	50	Leptomeningitis
2	1st	Turbid	+	0.09	0.031	++	1,510	30	Leptomeningitis
3	1st	Cloudy turbid	+	0.07	0.028	+	690	104	Leptomeningitis
4	2d	Cloudy turbid	+	0.15	0.041	+	320	60	Leptomeningitis
5	2d	Turbid	Gelatinous character	0.21	0.023	++	1,030	168	Leptomeningitis

EXPERIMENT WITH STAPHYLOCOCCUS CITREUS

Rabbits are inoculated with 0.3 c.c. of suspension of *Staphylococcus citreus.* (The intradermal injection with 0.1 c.c. of this suspension causes a small nodule with a central pustule to form in a rabbit after twenty-four hours.) Ataxia occurs on the first or the second day. Definite paralysis is seen on the third day. Necropsy reveals similar phenomena to those of pyogenic meningitis due to *Staphylococcus aureus*. The results are given in Table 7.

TABLE 7.—*Experiments with Staphylococcus citreus*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm. Polymorphonuclear	Cells per C. Mm. Lymphocyte	Remarks
1	1st	Cloudy turbid	Gelatinous character	0.16	0.034	++	1,088	203	Leptomeningitis
2	1st	Cloudy turbid	+	0.23	0.025	++	2,099	254	Leptomeningitis
3	2d	Turbid	+	0.096	0.021	++	1,088	310	Leptomeningitis
4	3d	Cloudy turbid	+	0.037	0.034	++	2,034	105	Leptomeningitis
5	3d	Turbid	Gelatinous character	0.19	0.031	++	899	231	Leptomeningitis
6	4th	Turbid	Gelatinous character	0.20	0.025	++	1,238	209	Leptomeningitis

EXPERIMENT WITH B. INFLUENZAE

Rabbits are inoculated intraspinally with 0.3 c.c. of suspension of *B. influenzae*. One culture on blood agar is suspended in 6.0 c.c. of 0.65 per cent. sodium chlorid solution. After a few hours, cerebral symptoms begin, which, in a few days, terminate in death. On necropsy the pia mater of the brain and the spinal cord are found intensely hyperemic, this being most marked at the convexity of the brain and the spinal cord. Microscopic changes in the pia mater are attended by hyperemia, and infiltration with leukocytes. Hemorrhages are found in the meninges. The results are shown in Table 8.

TABLE 8.—*Experiments with B. Influenzae*

Rabbit	Day of Disease	Appearance	Clot Formation	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm. Polymorphonuclear	Cells per C. Mm. Lymphocyte	Remarks
1	1st	Cloudy turbid	Gelatinous character	0.16	0.021	++	2,038	108	Leptomeningitis
2	1st	Cloudy turbid	+	0.23	0.034	++	1,039	201	Leptomeningitis
3	1st	Turbid	+	0.16	0.041	++	2,000	103	Leptomeningitis
4	2d	Turbid	+	0.09	0.026	+	1,238	86	Leptomeningitis
5	2d	Cloudy turbid	+	0.34	0.031	++	893	69	Leptomeningitis
6	3d	Turbid	+	0.21	0.028	++	2,136	263	Leptomeningitis

As these tables show, the cerebrospinal fluid of the rabbit, in which purulent meningitis due to pyogenic organisms has been produced experimentally, is opaque or purulent and shows an increase in the amount of albumin and globulin. The sugar content rapidly decreases. It shows a great predominance of polymorphonuclear cells. It may contain actual fragments of purulent material, which soon sink to the bottom. A marked clot formation of gelatinous character is always present.

SUMMARY

Subdural inoculation of virulent pyogenic organisms (pneumococci, *B. coli, B. influenzae, B. pyocyaneus,* streptococci and staphylococci) by an atlanto-occipital injection causes purulent meningitis in rabbits. The picture of the spinal fluid of the infected rabbit closely resembles that of purulent meningitis in human beings.

THE PRODUCTION OF TUBERCULOUS MENINGITIS IN THE RABBIT AND THE CHANGES IN ITS CEREBROSPINAL FLUID *

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Experimental meningitis, especially tuberculous meningitis in animals, has attracted little attention in the field of medicine. The first work on the subject was that done by Manwaring [1] in 1915. He succeeded in producing in dogs and in monkeys infection of the meninges, by injecting suspensions of tubercle bacilli into the subdural space through a trephine opening in the cranium. With this exception, we have been able to find no instance of tuberculous meningitis experimentally produced.

The work embodied in this paper is part of the study of experimental meningeal infection in the rabbit.

The experiments were made on adult rabbits and consisted, first, in producing tuberculous infection of the meninges, and second, in confirming the peculiar changes in the cerebrospinal fluid.

THE NORMAL CEREBROSPINAL FLUID OF THE RABBIT

Except in monkeys and in human beings, lumbar puncture is almost impossible in animals. In order to secure the cerebrospinal fluid from the subarachnoid space of the rabbit, a puncture needle is introduced into the space between the atlas and the posterior occipital tuberosity. The skin should previously be cleansed. The needle is introduced in the median line in a slightly upward direction. After passing through the rather tough intervening tissue, the sudden cessation of resistance announces the entrance of the point of the needle into the subcerebellar cisterna and then the spinal fluid is allowed to escape, or is drawn off, slowly but continuously, to the amount, as a rule, of 1 c.c. With a little practice, the atlanto-occipital puncture in the rabbit is easily and successfully made in every case.

By the above mentioned technic we have examined the normal fluid of about thirty rabbits. The results are briefly summarized as follows:

The normal cerebrospinal fluid of the rabbit is a perfectly clear and colorless liquid of low specific gravity, usually about 1.005; its reaction is faintly alkaline. Albumin is present in a very small amount, averaging

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* Received for publication, Dec. 20, 1923.

* From the Department of Pediatrics of the Medical College, the Kyoto Imperial University.

[1] Manwaring, W. H.: J. Exper. Med. **15**:1, 1915.

about 0.015 to 0.019 per cent. Globulin is normally absent. The average amount of sugar is 0.054 per cent. (after the microdetermination method of Bang). The cellular constituents are extremely scanty, averaging from about zero to ten cells per cubic millimeter and consist of lymphocytes. Polymorphonuclear cells are absent. If the fluid is allowed to stand, clot formation is not seen. The total amount present is generally about from 1.5 to 2.0 c.c.

EXPERIMENTAL TUBERCULOUS MENINGITIS IN THE RABBIT

To produce tuberculous meningitis in the rabbit, we introduced the suspension of tubercle bacilli into the subarachnoid space by the atlanto-occipital injection. The cerebrospinal fluid was withdrawn usually to an extent somewhat larger than the amount of suspension to be injected. Several strains of tubercle bacilli of the human, bovine, or avian types were employed. The inoculation material was prepared by diluting emulsions of the cultures, with 0.65 per cent. saline solution, which produced the desired turbidity. The amount of suspension usually injection varied from 0.25 to 0.3 c.c. The rabbit did not develop any visible reaction in all instances after the injection of the suspension.

The inoculation of virulent tubercle bacilli into the subarahnoid space of the rabbit by the above mentioned technic, produces a disease characterized by an incubation period of from six to fifteen days, followed by a period of cerebral symptoms that terminate in death.

The symptoms and the course of the disease in the rabbit are as follows:

The animal in the incubation period is apparently normal. Head tremor, rigidity of the neck and the back muscles, head retraction, ataxia, and the convulsion and paralysis of legs characterize the period of cerebral symptoms. The animal gradually becomes emaciated and finally collapses.

The most striking meningeal changes revealed by necropsy are miliary tubercles and inflammatory exudate. The tubercles are found chiefly at the base of the cerebrum and cerebellum; somewhat less frequently and less numerous on the convexity and on the spinal cord. The pia mater was congested everywhere, and appeared hazy and opaque. The other organs of the body show no characteristic change.

The symptoms and the clinical course depend on the dosage and virulence of the cultures injected. With a very virulent culture, death occurs rapidly. With less virulent cultures, the course of the disease is prolonged.

All the experiments were repeated with nearly uniform results. The following examples, selected from many experiments, will serve for demonstration purposes.

EXPERIMENT WITH HUMAN TUBERCLE BACILLI

RABBIT 1.—Weight 2,150 gm. was inoculated with 0.3 c.c. of suspension of human tubercle bacilli. (The intradermal inoculation of 0.1 c.c. of this suspension caused a small indurated nodule to form in a guinea-pig after five days, which later softened and then formed an abscess; this abscess opened externally leaving an ulcer.) The animal showed an incubation period of ten days; the cerebral symptoms, such as head tremor, head retraction and ataxia, began on the tenth day; definite paralysis on the twenty-fifth day; with death on the thirtieth day.

Necropsy showed numerous miliary tubercles in the entire meninges. The tuberculous nodules were more extensive in the region of the blood vessels and about the cranial nerves at the base. Microscopic examination of the pia showed marked tuberculous lesions. Abdominal and thoracic viscera were negative.

EXPERIMENT WITH BOVINE TUBERCLE BACILLI

RABBIT 2.—Weight 2,000 gm., was inoculated with 0.3 c.c. of suspension of bovine tubercle bacilli. (The intradermal inoculation of 0.1 c.c. of this suspension caused a small indurated nodule to form in a guinea-pig after three days, which became an abscess after seven days.) After seven days the rabbit became excitable, after ten days, ataxic and on the fifteenth day paralysis of the legs occurred. The animal succumbed on the twentieth day after inoculation.

Macroscopically, necropsy showed numerous miliary tubercles in the meninges, especially at the base of the brain. Microscopic lesions of the pia were found in the brain and cord. There was no visible change in the viscera.

EXPERIMENT WITH AVIAN TUBERCLE BACILLI

RABBIT 3.—Weight, 2,300 gm., was inoculated with 0.3 c.c. of suspension of avian tubercle bacilli. (Three milligrams of avian tubercle bacilli were emulsified in 3 c.c. of 0.6 per cent. sodium chlorid solution.) After six days the animal showed head retraction, and on the tenth day ataxia and paralysis. Death occurred in collapse on the fifteenth day. Miliary tubercles were seen in the meninges, the phenomenon being most marked at the base of the brain. There were no gross changes in the other organs.

THE CHANGE IN THE CEREBROSPINAL FLUID IN TUBERCULOUS MENINGITIS IN THE RABBIT

At a varying period after the intradural inoculation with tubercle bacilli, we have examined the cerebrospinal fluid in rabbits. In the examination of the cerebrospinal fluid, attention was paid to the estimation of the amount of albumin, globulin and sugar, the number of cells per cubic millimeter, the type of cells present, and the clot formation. Sugar was estimated by the microdetermination method of Bang, and globulin was tested by the butyric acid method of Noguchi, and the relative strength of the reaction noted. The results are recorded in Tables 1, 2 and 3.

As these tables show, the changes in the cerebrospinal fluid in tuberculous meningitis in the rabbit are peculiar to this disease. The fluid is more or less turbid and increases in the amount of albumin and globulin. The sugar content always decreases. In the early stage of the disease, the white cells increase in number, but lymphocytes are

TABLE 1.—*Experiments with Human Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	5th	Turbid	0.795	0.042	+	409	680	+
2	7th	Cloudy turbid	0.820	0.046	+	86	563	+
3	7th	Turbid	0.53	0.039	++	123	385	+
4	10th	Cloudy turbid	0.29	0.035	+	0	708	Gelatinous character
5	13th	Cloudy turbid	0.82	0.02	++	0	982	Gelatinous character
6	15th	Turbid	0.13	0.031	++	0	1,085	Gelatinous character
7	20th	Cloudy turbid	0.83	0.01	++	0	960	+
8	16th	Turbid	0.036	0.005	++	0	1,204	+
9	16th	Cloudy turbid	0.039	0.003	++	0	765	Gelatinous character
10	20th	Cloudy turbid	0.042	0.001	++	0	1,060	+
11	31st	Cloudy turbid	0.12	0.01	+	0	618	+
12	35th	Cloudy turbid	0.18	0.035	++	0	971	Gelatinous character
13	35th	Turbid	0.15	0.033	++	0	550	Gelatinous character

TABLE 2.—*Experiments with Bovine Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	4th	Slightly turbid	0.025	0.05	+	8	93	—
2	4th	Turbid	0.035	0.045	+	36	103	—
3	7th	Turbid	0.041	0.039	+	4	204	—
4	15th	Cloudy turbid	0.069	0.026	+	0	736	+
5	15th	Cloudy turbid	0.078	0.032	+	0	1,090	Gelatinous character
6	20th	Cloudy turbid	0.098	0.03	+	0	132	Gelatinous character
7	25th	Cloudy turbid	0.073	0.01	+	0	693	+
8	28th	Cloudy turbid	0.125	0.031	+	0	1,056	+

TABLE 3.—*Experiments with Avian Tubercle Bacilli*

Rabbit	Day of Disease	Appearance	Albumin, per Cent.	Sugar, per Cent.	Globulin	Cells per C. Mm.		Clot Formation
						Polymorphonuclear	Lymphocyte	
1	4th	Slightly turbid	0.054	0.035	+	210	280	+
2	4th	Slightly turbid	0.024	0.045	+	28	180	+
3	7th	Turbid	0.05	0.04	+	130	200	+
4	7th	Turbid	0.062	0.032	+	80	320	+
5	11th	Turbid	0.051	0.04	+	2	350	+
6	15th	Cloudy turbid	0.086	0.039	+	0	680	+
7	15th	Cloudy turbid	0.12	0.023	+	0	1,073	+
8	18th	Turbid	0.16	0.031	+	0	679	+
9	20th	Turbid	0.096	0.03	+	0	1,079	+

still predominant. Polymorphonuclear leukocytes decrease, and gradually the percentage of lymphocytes increases. In the later period the type of cells present in the fluid is always mononuclear. Clot formation is present. Sometimes it shows a marked gelatinous character.

The picture closely resembles that of tuberculous meningitis in human cases.

SUMMARY

Subdural inoculation of tubercle bacilli by atlanto-occipital injection produces in the rabbit tuberculous meningitis, followed by paralysis and death. The changes in the cerebrospinal fluid are peculiar. There is an alteration in the chemical and cellular constituents.

UROBILIN EXCRETION IN THE ANEMIAS OF INFANTS AND CHILDREN *

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AND
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It is now well established that the amount of urobilin and urobilinogen in the stools is a rough index of the amount of blood destruction going on in the body. Since no large number of cases of anemia in children has been studied as regards their urobilin excretion, it seemed worth while to undertake such a study. Our plan was to determine, if possible, whether certain of the forms of anemia met with in childhood might be differentiated from others by their pathogenesis. In other words, are there some forms of anemia in infancy characterized by excessive blood destruction? It is well known that in the anemia seen in cases of hemolytic icterus, there is excessive blood destruction, evidenced by an unusually large amount of urobilin in the stools and urine. Hemolytic icterus is the best example of an anemia due to blood destruction and it seemed likely that other forms of anemia might perhaps be due to a similar process. Moreover, we felt that in studying the pathogenesis of infant anemias we might possibly be able to throw a little more light on their classification. Merely clinical classifications of anemia in childhood are very unsatisfactory, and much might be gained if we knew more about the exact process by which the anemia is brought about.

It was especially in the group of anemias known as "alimentary" that we hoped to get some positive results. It may be well to recapitulate briefly the present ideas concerning this group of cases. The fact that certain infants developed anemia when fed a diet consisting almost exclusively of milk, led Czerny and his school to make a separate group in the anemias entitled "Alimentary anemia." For a time it seemed to be proved that the diet alone was responsible for the change in the blood. However, many children were observed who, fed on the same one sided diet, failed to become anemic. Controversy therefore exists chiefly in regard to the question as to whether food alone can produce this type of anemia. Kleinschmidt believes that "A certain congenital disposition" must be associated with inadequate diet and that more than one type of faulty diet may be responsible for the anemia. French authors also found anemia occurring frequently in twins, and in prema-

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* Received for publication, Jan. 21, 1924.

* From the pediatric service of Mount Sinai Hospital.

ture and debilitated infants. The blood picture in these cases is similar to that found in chlorosis of adults, a greater decrease in the percentage of hemoglobin than in the number of red cells, and for this the term "Anémie, a type chlorotique" was proposed. This classification refers merely to the morphology of the blood and suggests nothing in regard to etiology.

On the other hand, Czerny and his followers laid the blame for this alimentary anemia not only on the food, but on a particular kind of food, namely fat. They believed that an excess of milk fat in infants' diets led to a destruction of red cells and thus to anemia. They went so far as to postulate that it was the fatty acids which broke down the red cells, basing this theory partly on the marked hemolytic action of oleic acid in vitro. That the erythrocytes were not destroyed in the circulating blood was proved by the absence of hemoglobinuria. Most likely the destruction must take place in the liver and spleen; that is. in those centers where normal blood destruction occurs. To prove this they looked for and found deposits of hemosiderin in the liver and spleen. Further, to establish this hypothesis they tried to show that there was evidence of excessive blood destruction. This link in the chain of evidence was furnished by Glanzman,[1] who published results showing excessive excretion of urobilinogen in the stools of children suffering from alimentary anemia.

Glanzman's results, however, comprise but a few cases, and the method used by him is open to question. He apparently determines only the urobilinogen and not the urobilin. This would necessarily lead to great error since the one substance may be transformed into the other in the intestinal canal. Moreover, many of his results seem to be based on the examination of a single day's feces. The excretion of urobilin and urobilinogen is so irregular that very great differences are found in the amounts excreted on consecutive days. To get an adequate idea of the total excretion one must therefore make determinations over a number of days; as many, even, as six or seven.

Although not at all convincing, Glanzman's results are interesting and prompted us to investigate the urobilin and urobilinogen excretion in similar cases.

The method used by us[2] for urobilin determination was that of Wilbur and Addis.[3] This method is admittedly a rough one, and will certainly fail to show very small changes in the amount of urobilin present in the stools. (By urobilin is meant the sum total of urobilin and urobilinogen found in the stools.) For larger variations it has proved itself a good method. Since many factors, such as the destruction of urobilin in the intestine, or its reabsorption from the intestine, combine to make the total urobilin excretion only roughly proportional to the amount of blood destruction, only a very pronounced increase in the urobilin found in the stool may be accepted as proof of a hemolytic process.

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[1] Glanzman: Jahrb. f. Kinderh. **84**:95, 1916.

[2] A Smith & Haensch spectroscope, with adjustable slit, was used. Illumination was obtained by enclosing a Mazda electric bulb in a box completely closed, except for a small opening for insertion of the spectroscope.

[3] Denzer, B. S., and Merritt, K. K.: The Urobilin Content of the Stools of Normal Infants, Am. J. Dis. Child. **27**:297 (April) 1924.

As no figures were available for urobilin excretion of normal children over 1 year of age, preliminary examinations of normal children were made. The results are shown in Table 1. The variations are wide, which was to be expected when obtained by the method of Wilbur and Addis. However, only the upper limit of normal is of importance in the consideration of the urobilin of the stools as an indicator of the degree of blood destruction. It may be said, then, that under 6 years of age the normal urobilin does not exceed 800 dilution units, and between 6 and 11 years it does not exceed 1,400 units.

TABLE 1.—*Excretion of Urobilin in the Stools of Normal Children*

Case	Period of Observation, Days	Age	Average Total Urobilin Values
1	6	18 months	287
2	6	2 years 2 months	500
3	5	3 years	147
4	6	3 years 6 months	283
5	7	3 years 6 months	428
6	3	5 years	733
7	4	6 years	750
8	6	6 years	798
9	6	6 years	1,000
10	6	7 years	1,167
11	6	8 years	870
12	6	10 years	1,180
13	7	11 years	1,345
14	6	11 years	775

We have examined, in all, twenty-one children suffering from various forms of anemia and from diseases of the hepatosplenic system. Table 2 shows the various illnesses and the laboratory findings. It will be seen that only one case showed a really definite increase in the urobilin excretion. This patient was suffering from typical congenital hemolytic jaundice. The urobilin excretion was more than five times the normal amount and following splenectomy it dropped promptly to almost within normal limits. There were three cases that showed a slightly excessive excretion (the last three in Table 2). The urobilin values in these cases were considerably less than double the normal amount. Two were obscure conditions, affecting liver and spleen, and the third was Gaucher's disease. So far as we know, excessive blood destruction has not been found previously in Gaucher's disease, and a greater number of cases would have to be studied to determine its

Table 2.—*Excretion of Urobilin in Alimentary Anemia and Other Pathologic Conditions*

Name	Sex*	Age	Period of Observation, Days	Urobilin Values	Hemoglobin, per Cent.	Diagnosis	Remarks
Alimentary Anemia							
L. B.	♀	18 mo.	5	165	30	Anemia, rickets, nasopharyngitis	Diet: milk and cereal. Repeated upper respiratory infection probably also an etiologic factor
R. R.	♂	15 mo.	12	391	40	Nasopharyngitis, rickets	Slow improvement under iron therapy
E. O.	♂	2¾ yr.	6	184	24	Anemia	Diet: milk and orange juice. Refused all solid food. Premature baby. Predisposition (prematurity) and food only etiologic factors. Marked improvement with iron; hemoglobin to 70 per cent. Systolic cardiac murmur disappeared
G. K.	♀	9 mo.	4	86	14	Anemia	Diet: milk, water and sugar until few weeks previously; cereal and little vegetable added. Full term. Pertussis at four months. Blood transfusion and iron given. In two weeks hemoglobin 40 per cent.
Congenital Hemolytic Jaundice							
E. S.	♀	6 yr.	7	4,862	45	Congenital hemolytic jaundice	Spleen removed. Normal urobilin about 1,400 or less
Postoperative			6	911			
Miscellaneous Conditions							
J. B.	♂	4 yr.	6	247	59	Rheumatic carditis	Normal urobilin. Progressive anemia. Hemoglobin fell to 48 per cent.
M. S.	♀	8 yr.	7	767	68	Malignant endocarditis	Normal urobilin. Progressive anemia. Hemoglobin fell to 47 per cent.
M. D.	♂	2¾ yr.	6	575	39	Anemia following pneumonia	Urobilin normal. Estimations made after pneumonia. Progressive anemia during and after pneumonia
G. N.	♀	12 yr.	7	864	39	Endocarditis; etc.	Normal urobilin. Large spleen and liver
R. H.	♀	10 mo.	8	148	60	Tuberculosis	Normal urobilin. Progressive anemia. Hemoglobin fell to 49 per cent.
R. P.	♀	10 yr.	6	1,174	..	Trichinosis	Normal urobilin
M. P.	♀	8 yr.	6	925	..	Trichinosis	Normal urobilin
M. P.	♀	10 yr.	7	584	35	Aplastic anemia(?)	Normal probilin
A. S.	♂	6 yr.	7	682	74	Hemorrhagica purpura	Normal urobilin
F. F.	♀	8 yr.	6	1,070	62	Purpura hemorrhagica	Normal urobilin. No decrease. postoperative splenectomy
Postoperative			9	1,079			
J. R.	♂	6½ yr.	6	927	96	Splenomegalic cirrhosis (?)	Normal urobilin
H. P.	♀	9 yr.	4	425	93	Gaucher's disease (?)	Normal urobilin. Diagnosis not proved; neither splenectomy or puncture done
E. G.	♂	8 yr.	7	870	..	Hepatic lymphangioma (?)	Normal urobilin
Slightly Increased Urobilin Values							
F. K.	♂	2½ yr.	8	816	75	Splenomegalic cirrhosis (?)	Normal urobilin value not above 800
M. R.	♂	9 yr.	6	2,233	72	Splenomegaly (?)	Normal urobilin value not above 1,400. Diagnosis never established. Case not followed
F. R.	♀	3 yr.	6	1,352	66	Gaucher's disease	Normal urobilin value not above 800. Spleen removed; proving diagnosis
Postoperative			7	842	82		

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* In this column, ♀ indicates female, ♂ male.

significance. Possibly any extensive enlargement of the spleen might be sufficiently associated with its blood destructive function to account for the slightly higher values found in these three cases.

In the four cases which we have grouped under the heading of alimentary anemia, no increase in urobilin excretion could be found. This may be due, possibly, to the methods employed, since the blood destruction may proceed at a very slow rate producing a smaller amount of urobilin in the stool at any one time than the method is able to show. It would seem, however, that if an excessive blood destruction accompanied the severe types of infantile anemia, a patient such as G. K. should have presented some evidence of increased urobilin in the stool. This infant with a hemoglobin percentage of 14 failed to show even a slight increase in the urobilin excretion. It seems fair to conclude, then, that rapid and excessive blood destruction is not an important factor in the anemias of infancy (the chlorotic and alimentary anemias).

SUMMARY

1. The sum of the urobilin and urobilinogen excretion in the stools of normal children, obtained by the method of Wilbur and Addis, is less than 800 dilution units for children under 6 years of age; and less than 1,400 units for children under 11 years of age

2. There is no evidence of excessive blood destruction in the anemias of infancy as indicated by the urobilin excretion in the stools, determined by the method of Wilbur and Addis.

THE CALCIUM CONTENT OF BREAST MILK IN RELATION TO RICKETS *

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The rôle of the calcium ion in the metabolism of rickets has for a good many years formed the keystone of the arch in the study of this disease. The conception, recently advanced by Howland and his associates, of the existence of two forms of rickets, the low calcium and the low phosphorus types, is based chiefly on the chemical study of the blood.

Experimentally, the feeding of low phosphorus diets to animals leads to the production of true rickets, whereas low calcium diets lead not to true rickets, but to osteoporosis. It is a fact that in all forms of rickets the body as a whole shows a marked lowering of its calcium content.

Recently, one of us [1] has shown that in the breast milk on which babies develop rickets there was no reduction in the inorganic phosphate constituents, and it seemed worth while to study also the calcium content. To this end mother's milk was obtained from those attending the newly born service of Touro Infirmary, simultaneous observations being made on the infants and in a few instances the clinical examinations were checked by roentgenograms of the wrists. Where, however, the roentgen ray showed no evidence of rickets, while the clinical findings indicated its presence, we have given preference to the clinical evidence, for we agree with Hess [2] that the roentgen ray frequently lags behind the clinical examination in furnishing evidence of the earliest beginnings of rickets.

It must be stated that all the infants in this study were receiving, in addition to their regular nursings, a daily ration of cod liver oil emulsion (one coffeespoonful three times a day). It might be said, therefore, that those infants who developed rickets, in spite of cod liver oil administration, did so on a very gross deficiency of the essential element in the breast milk, if such a deficiency exists at all.

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* Received for publication, Feb. 27, 1924.

* From service of the newly born, Touro Infirmary, and the School of Medicine of Tulane University of Louisiana.

[1] Von Meysenbug, L.: The Inorganic Phosphate Content of Breast Milk of Mothers with Normal and with Rachitic Infants, Am. J. Dis. Child. **24**:200 (Sept.) 1922.

[2] Hess, A. F.: Newer Aspects of the Rickets Problem, J. A. M. A. **78**:1177 (April 22) 1922.

METHOD

The milk was secured as uniformly as possible from all mothers in the following way: the infant was allowed to nurse one breast for ten minutes, at the end of which time approximately ½ ounce (15 c.c.) of the strippings was expressed manually into a clean, dry container. An equal quantity was obtained of the foremilk from the other breast, the two thoroughly mixed and kept in the refrigerator until analyzed.

The calcium determinations were carried out as follows: 10 c.c. of milk were pipetted into a 20 c.c. volumetric flask containing about 6 c.c. of 20 per cent. trichloracetic acid (calcium free) and heated in a boiling water bath from fifteen to twenty minutes until a brownish color indicated the caramelization of the lactose, when coagulation of the proteins was usually complete. The flask was cooled and made up to volume. Filtration through double acid washed filter paper gave a crystal clear, slightly yellowish filtrate. Five cubic centimeters of filtrate were pipetted into a 15 c.c. graduated centrifuge tube containing 2 c.c. of saturated ammonium oxalate solution and one drop of methyl red. The tube was rotated so as to mix the fluids, and enough of 20 per cent. sodium acetate was added (usually 3 c.c. sufficing) to give a p_H of 5.0 as compared with the color charts of Clark.[3] This p_H is, according to Clark, the optimum for the precipitation of calcium.[4]

Table 1.—*Normal Babies*

Date	Patient	Age	Ca, Mg. per 100 C.c. Milk	Date	Patient	Age	Ca, Mg. per 100 C.c. Milk
12/ 9/22	M. G.	14 days	32.0	1/30/23	G. R.	1 mo.	35.6
12/30/22	J. S.	4 mos.	31.3	2/ 1/23	A. M.	8 wks.	37.4
12/30/22	C. A.	14 mos.	23.7	2/ 1/23	H. A.	2 mos.	35.4
1/ 2/23	E. P.	5 mos.	30.4	2/15/23	E. M.	2 mos.	39.5
1/ 4/23	D. McD.	4 wks.	32.0	3/ 6/23	C. M.	7 mos.	24.3
1/ 9/23	C. D.	5 wks.	31.0	4/ 5/23	E. S.	4½ mos.	31.9
1/ 9/23	L. W.	6 wks.	33.9	4/19/23	B. G.	5 mos.	34.0
1/16/23	J. V.	8 mos.	32.9	6/21/23	B. D.	2 mos.	40.0
1/20/23	H. T.	5 wks.	32.9	6/28/23	M. H.	2 mos.	31.9
1/27/23	V. H.	8 wks.	30.2				
Average							32.6

The tube was stoppered, set aside over night and then centrifuged at high speed for ten minutes. Supernatant fluid was siphoned off and the precipitate washed with 2 per cent. of ammonia water. The washing and centrifuging were repeated three times. Solution of the precipitate was effected with 2 c.c. approximately double normal sulphuric acid, the tube heated in boiling water and the calcium oxalate titrated against hundredth normal potassium permanganate solution,

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3. Clark, Wm.: The Determination of Hydrogen Ions, Baltimore, Williams & Wilkins, 1920.

4. Clark, G. W.: The Micro Determination of Calcium in Whole Blood, Plasma, and Serum by Direct Precipitation, J. Biol. Chem. **49**:487 (Dec.) 1921.

correction being made for the blank. Analysis of known calcium solutions showed this method to be accurate within ± 5 per cent. The results of the milk analysis are set forth in the tables.

Table 1 shows the average of nineteen "normal" milks to be 32.6 mg. per hundred cubic centimeters with extremes of from 23.7 to 40.0 mg.

Table 2.—*Rachitic Babies*

Date	Patient	Age	Rickets Clinically	Rickets by Roentgen Ray	Ca, Mg. per 100 C.c. Milk
1/ 9/23	A. P.	5 mos.	++	....	24.1
1/ 9/23	I. S.	5 mos.	+±	....	27.0
1/12/23	W. McC.	9 mos.	++	....	29.4
1/12/23	H. H.	8 mos.	+±	....	22.2
1/12/23	A. J.	4 mos.	+++	....	19.3
1/12/23	R. C.	14 mos.	+	....	20.1
1/16/23	A. L.	3 mos.	+	....	22.4
1/16/23	A. B.	4 mos.	±	....	26.2
1/16/23	P. T.	2 mos.	+	....	22.4
1/20/23	R. J.	11 mos.	+±	....	28.5
1/20/23	L. J.	5 mos.	+	....	31.5
1/20/23	E. R.	5 wks.	±	....	29.4
1/23/23	J. B.	11 mos.	+	....	23.9
1/25/23	A. A.	4 mos.	±	....	33.9
1/25/23	C. McD.	3½ mos.	+	...	31.0
1/27/23	E. H.	12 mos.	++	....	27.2
1/27/23	E. F.	3 mos.	+	....	29.4
1/30/23	C. M.	4 mos.	±	....	30.3
2/ 1/23	U. G.	2 mos.	+	....	30.6
2/ 3/23	E. J.	4 mos.	±	....	23.8
2/ 3/23	W. B.	8 mos.	+	0	39.6
2/ 3/23	A. H.	3 mos.	±	healing	32.7
2/ 6/23	D. T.	9 mos.	±	±	19.2
2/ 8/23	V. L.	6 mos.	++	+	31.4
2/ 8/23	P. V.	4 mos.	±	0	34.4
2/10/23	D. F.	7 mos.	+	±	20.9
2/10/23	B. C.	7 mos.	+	0	26.9
2/10/23	J. A.	2 mos.	±	0	22.1
2/15/23	E. J.	5 mos.	+±	....	29.1
2/15/23	U. J.	3 mos.	++	0	32.1
2/15/23	M. M.	7 mos.	+	+	26.5
2/17/23	D. S.	3 mos.	+	+	31.7
2/20/23	T. L.	2 mos.	+±	0	33.9
2/20/23	S. E.	8 mos.	+	0	21.0
2/22/23	D. J.	7 mos.	++	....	23.2
2/22/23	A. H.	3 mos.	+	0	26.5
2/22/23	P. B.	2 mos.	++	0	23.0
2/24/23	V. B.	7 mos.	+	0	26.5
2/24/23	K. M.	3 mos.	±	....	35.5
2/27/23	S. S.	6 mos.	±	0	36.3
3/ 1/23	W. S.	5 mos.	+	+	27.6
3/ 1/23	W. B.	4 mos.	++	+	18.4
3/ 3/23	D. L.	7 mos.	+	....	19.9
3/ 8/23	E. R.	10 mos.	+	+	27.3
3/ 8/23	H. T.	3 mos.	+	+	27.8
3/10/23	P. T.	5 mos.	++	±	30.2
3/29/23	R. E.	3 mos.	+	0	33.1
5/ 3/23	H. R.	5 mos.	+	....	24.2
5/17/23	G. M.	2 mos.	++	....	31.6
5/17/23	E. S.	5½ mos.	+	....	30.0
6/21/23	V. C.	3½ mos.	±	....	28.0
Average..					27.5

The average of the "rachitic" milks, as collected in Table 2, is 27.5 mg. with extremes of from 18.4 to 39.6 mg. With a view to correlating the severity of the rickets with the milk calcium we have calculated the averages as follows: When the clinical evidences of rickets is ± (based chiefly on the degree of the beading) the average is 29.3 mg. where rickets is + it is 26.8 mg.; for + ± and + +, 26.8 mg. The only + + + case had 19.3 mg.

TABLE 3.—*Averages for Different Periods*

Period	Number of Analyses	Ca, Mg. per 100 C.c.
1 – 3 months..	30	31.1
4 – 7 months..	28	28.0
8 months – 1 year..................................	12	26.2

TABLE 4.—*Calcium Content of Mature Breast Milk*

Author	Ages	Ca, Mg. per 100 C.c.
Schloss..	2 – 6 mos.	29.7
Pelka...	....	33.5
Holt, et al.	1 –10 mos.	33.3
Abderhalden...	2 – 3 mos.	34.6
Blanberg..	....	27.9
Denis *...	....	29.5
Von Meysenbug...	1 –12 mos.	32.6

* Unpublished work.

TABLE 5.—*Averages for Different Periods**

	Number of Analyses	Ca, Mg. per 100 C.c.
Colostrum (1-12 days)..............................	5	31.6
Transition (12-30 days).............................	6	29.0
Early mature (1-4 months).........................	9	34.5
Middle mature (4-9 months).......................	8	32.5
Late milk (10-20 months)..........................	10	27.7

* Computed from Table of Holt et al.[5]

TABLE 6.—*Average of Milks of White and Colored Mothers*

White			Colored			
32.0	30.6	35.6	30.4	32.8	23.8	23.0
31.3	39.6	36.3	30.9	28.5	32.7	18.4
23.8	34.4	27.6	24.1	31.5	19.1	19.9
33.2	26.9	27.3	27.0	29.4	31.4	33.1
30.0	22.1	30.2	33.9	23.9	20.9	24.3
32.9	26.5	32.0	22.2	33.9	29.1	27.8
30.3	33.9	30.0	19.6	31.0	39.5	34.0
37.4	26.5	40.0	20.1	27.2	32.1	24.2
35.4	26.6	28.0	22.4	29.4	31.7	31.6
		——	26.4	30.2	21.0	31.9
Average...............		31.1 mg.	22.4	35.6	23.2	——
			Average............................			27.3 mg.

In Table 3 we have grouped the milks according to the ages of the infants (stage of lactation). This table includes all the milks, "normal" as well as "rachitic."

Table 4 comprises breast milk calcium as found by different investigators, taken from Holt.[5]

For comparison with our results of analyses at progressing stages of lactation we have inserted Table 5 taken from Holt.

In Table 6 we have grouped all the milks of white and colored mothers separately and the average of the two show 31.1 mg. for milk of the white mothers and 27.3 mg. for the milks of the colored mothers.

COMMENT

It will be seen from the Tables that milks from some of our severest cases of rickets showed calcium content well within the range for the "normal" milks, two being higher than the normal average. On the other hand, nowhere do we find in the controls the low extremes that we find in the rachitic group. Whether or not some of our rachitic cases showing high milk calciums belonged in the low phosphorus group could only have been determined by calcium and phosphorus determinations of the infants' blood.

We do not feel that the routine administration of cod liver oil to all the infants in this study has vitiated our results, for the infants developed rickets in spite of such administration, and obviously giving cod liver oil to the infant could in no way affect the calcium content of the mothers' milk.

As we have secured milks from only nineteen control cases, and as we have fifty-one test milks, it was thought that comparison of the two groups might not be fair. We, therefore, averaged the first nineteen milks of the rachitic group and found it to be 26.7 mg. calcium per hundred cubic centimeters, an average even lower than that of the entire series of fifty-one cases.

As colored babies are so prone to develop rickets we thought that there might be some reduction of the milk calcium in colored mothers. In a recent study of Burhaus and Smith[6] this was shown to be the case, the average for the milks of the white mothers being 30.79 mg.; for the milks of the colored mothers 25.41 mg. per hundred cubic centimeters. Our averages are 31.1 mg. for the white race, 27.3 for the colored race.

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[5] Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10:** 229 (Oct.) 1915.

[6] Burhaus, C. W., and Smith, D. N.: The Inorganic Constituents of Human Milk with Particular Reference to Racial Variations, Am. J. Dis. Child. **26:**303 (Oct.) 1923.

SUMMARY

In a study of the calcium content of breast milk we have found the average of "normal" milks to be 32.6 mg. per hundred cubic centimeters, with extremes of from 23.7 to 40.0 mg.

The "rachitic" milks averaged 27.5 mg. with extremes from 18.4 to 39.6 mg.

Grouping the milks according to the age of the infant we found the calcium content diminishes as lactation progresses.

The calcium content of milk from the white race as compared with that of the colored shows a reduction in the latter race.

SUBACUTE INTUSSUSCEPTION *

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The term subacute, in relation to intussusception, commonly describes a type of case in which symptoms have existed for at least a week, yet does not present the striking symptomatology manifested by the typical acute cases. Certain of these subacute cases offer difficult problems in diagnosis. As detailed descriptions of such cases in infants and young children are but rarely presented, the report of the four following cases seems of sufficient interest to merit publication.

REPORT OF CASES

Case 1.—*History.*—H. G., a girl, the second of two children, was breast fed exclusively for one month, and then because of failing lactation, five supplementary feedings of whole milk and barley-water mixtures were given in addition to three nursings. At 4 months of age the infant was brought to the outpatient department of the Babies' Hospital because of vomiting and diarrhea. The symptoms yielded promptly to dietary changes and the child gained normally in weight. At 6 months of age the weight was recorded as 14 pounds (6,350 gm.).

Present Illness.—On July 17, 1922, when 6 months of age, the infant was brought to the outpatient department by the mother, who stated that eight days previously the child had vomited and had passed four stools of bright red blood mixed with mucus, associated with severe colicky pains. The family physician in attendance at this time treated her with "powders." The bowels became constipated and enemas resulted in "black stools."

On the day of admission to the hospital the colicky pains were still present, but the patient did not look acutely ill nor was she dehydrated. The mother stated that constipation was present and that food was refused. A small greenish fecal stool of normal consistency was passed at the time of examination. This gave a positive guaiacum test for blood. Under ether anesthesia a sausage-shaped mass was readily felt in the right lower quadrant of the abdomen. The white blood cells numbered 23,000; the polymorphonuclears were 69 per cent.

Operation was immediately performed by Dr. Richard Bolling. Under ether anesthesia a right rectus incision was made, and an intussusception 12 inches (30 cm.) long was found. This began at the ileocecal valve and involved the appendix. There was some inflammation present but no necrosis was seen, and the intussusception was easily reduced. Two ecchymotic spots were seen in the mesentery. The ileum was sewed to the cecum for a distance of about 2 inches (5 cm.) with the idea of preventing recurrence. The incision was then closed and the patient made an uneventful recovery.

The infant has been seen repeatedly since the operation and appears to be normal in every respect.

Case 2.—A. L., a boy, aged 6 months, was admitted to the Babies' Hospital, March 7, 1922.

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* Received for publication, Feb. 11, 1924.

* Report of Four Cases from The Babies' Hospital Dispensary.

Previous History.—He was the youngest of four children, of healthy parents, born at term, with birth weight recorded as 9 pounds (4,082 gm.). He was nursed up to the onset of the present illness and throve in a normal fashion.

Present Illness.—Sixteen days prior to admission to the hospital the infant became suddenly ill. Bloody stools were noted at the onset, after which their character changed to a mixture of blood, mucus and feces, subsequently containing curds and mucus. Since then there had been six or seven watery stools daily but none contained any blood. The patient had been prostrated from the onset. The attending physician thought his symptoms were due to intestinal intoxication. His condition seemed to improve until five days before entering the hospital, when high fever began, which the physician believed to be due to meningitis. Prostration became more marked. This was associated with dyspnea and persistent vomiting of food and greenish material.

A diagnosis of peritonitis was then made and the child was referred to the Babies' Hospital.

Physical Examination.—On admission to hospital the child was moribund. The features were pinched, the expression was anxious and the true facies abdominalis was seen. The respirations were rapid; the vomiting of bile stained material occurred repeatedly. The temperature was 102.2. The abdomen was tense and much distended. The clinical diagnosis was general peritonitis. The infant died one hour after admission to the hospital.

Necropsy was performed by Dr. Martha Wollstein with the following findings: On opening the abdomen, the presenting loops of intestine were adherent to the abdominal wall and to each other by fibrinous adhesions which were easily broken down. The peritoneal cavity was found to be full of greenish, odorless pus in which there were large flakes of fibrin. There was an ileocecal intussusception present, into which the base of the appendix was disappearing. The outer surface of the tumor, which measured 7 by 4 cm., was red in color, but showed no signs of gangrene and was easily reducible. The colon below the tumor contained yellow, pasty feces and the small intestine above contained very loose fecal matter. The stomach contained bile-stained material; its mucosa and that of the duodenum were normal.

The anatomic diagnosis was ileocecal intussusception—not complete.

The history of sudden onset sixteen days before death with stools containing fresh blood, subsequently becoming fecal, made it appear that the original condition had been intussusception without complete obstruction, in which there had been a spontaneous, incomplete reduction.

Case 3.—E. G., a boy, aged 8 months, the youngest of three children, of healthy parents, was born at term, after a normal birth. He had been nursed every three hours, had gained in weight normally, and had never been ill.

Present Illness.—Eight days before admission to hospital the infant became restless, and subsequently passed four loose stools containing mucus. On that day he slept fairly well but during the night on three occasions vomited small amounts of food. The following morning he refused food, and again was quite restless and vomited a considerable amount of brown-stained material. Later in the morning, a large amount of bright red blood "gushed from the bowels," which was stated to have saturated three diapers and the mattress. No evidence of pain was noted and the child became drowsy. A physician called thought it was a case of "bloody dysentery" and prescribed medication. The following day the patient passed two bloody stools. Another physician was called five days later, but during this time there was a daily stool containing some blood. The day prior to admission to the hospital the patient had a normal stool which did not contain blood.

On the day of admission he had another blood stained stool, and vomiting was observed at four different times. It was also stated that he showed signs of great pain.

Physical Examination.—The infant, when presented for admission, was critically ill, in a comatose state, with ashy countenance, sunken eyes rolling from side to side, and a sunken fontanel admitting two finger tips. The abdomen was soft; the liver and the spleen could not be palpated. Although no definite mass could be palpated nor could any be felt by rectum, the whole picture of the illness and the manner of its development suggested the diagnosis of an invagination of the bowel.

Operation was performed by Dr. Bolling, eight days after the onset of symptoms. A right rectus incision was made and an intussusception was found which was markedly edematous. The head of the column was formed by the lower end of the cecum at a point opposite the ileocecal valve.

Immediately after the operation the child was in such good condition that he tried to sit up. Eighteen hours later he began to vomit and the pulse became small. The following day signs of obstruction became manifest with fecal vomiting. No fecal contents were withdrawn on irrigation of the colon. That evening there was a second operation for obstruction, and an ileus was found, the paralysis apparently being of toxic origin. An ileostomy was performed and a catheter was sewed into the ileum. The child remained in a critical condition for several days, but gradually improved and was discharged as cured. He has been seen at regular intervals since his discharge from the hospital and is doing well.

Case 4.—F. B., a boy, aged 8 years, walked into the outpatient department of the Babies' Hospital, Dec. 29, 1919, complaining of pain in the left side of the abdomen.

The family and past history were negative.

Present Illness.—For one week previous to admission to hospital he had four watery stools daily. His appetite was good. He had had intermittent pain in the abdomen but it was not severe enough to confine him to bed; in fact, he was running about as usual, bending over from time to time as the pain occurred. He had noticed a lump in the left side of abdomen but did not know how long it had been present. He had no symptoms referable to the urinary tract.

On the day before coming to the hospital he noticed that the stool was orange colored, of jelly-like substance; he had not noticed the presence of blood.

Physical Examination.—The boy was very pale. During the examination he vomited twice, and at intervals had severe colic in the left flank and the left lower quadrant of the abdomen.

There were no positive findings except in the abdomen, which was flat and soft. A firm, elongated, movable, slightly tender mass 3 by 2 inches (7 by 5 cm.) was palpated in the left lower quadrant, which followed the course of the descending colon or sigmoid. No other masses or tenderness were elicited. The liver, spleen and kidneys were not palpable.

The urinalysis was negative.

The white blood cells numbered 12,100, and polymorphonuclears were 69 per cent.

A diagnosis of intussusception was made, and the child was referred to the Presbyterian Hospital for operation as he was above the age limit of admission to the Babies' Hospital.

Operation was performed by Dr. Sidney Burnap eight days after onset. We are indebted to the Presbyterian Hospital for the following report: "Under ether anesthesia, an incision 5 inches (12 cm.) long was made through the right rectus, and a sausage-shaped mass was found in the left lumbar region extending as low as the brim of the pelvis upward toward the splenic flexure into the transverse colon. The omentum was adherent to it, with fresh adhesions, in the region of the splenic flexure. On reduction of the invagination, at the terminal portion corresponding to the part at which the intussusception began, which was situated close to the junction of the transverse colon with the splenic flexure, the colon was found to be markedly edematous and congested. This condition, however, subsided greatly on the application of hot towels. No necrosis was seen, the ileocecal junction was found to be normal, and the abdomen was closed."

The patient made an uneventful recovery, and is seen at regular intervals. He is in excellent health, although he complains occasionally of a slight vague pain in the abdomen.

COMMENT

The symptoms of acute intussusception in infants need no review. When a healthy nursing infant in the middle third of his first year suddenly develops pain of a paroxysmal character, accompanied by vomiting whenever food is taken, one naturally thinks first of intussusception. If bright red blood is passed by rectum it only remains to palpate the tumor to make certain of the diagnosis. The symptoms of the subacute type resemble the acute in most particulars except that they are more moderate in their manifestations, and for that reason the diagnosis may be unduly delayed. Three of the four cases here presented were treated for dysentery before admission to the hospital, and it is readily understood how such an error might be made unless the physician had the actual condition in mind. Nursing infants who have always been well are not immune to dysentery; and colic, vomiting, bloody stools and collapse may all be present when it occurs. Increase in pain, more frequent recurrence of the attacks of colic with profuse evacuation of blood and mucus following collapse point to invagination. General anesthesia is frequently necessary to secure sufficient muscular relaxation to establish the presence of a tumor. The vomiting in the subacute patients is not continuous, the loud shrieks due to pain are not noted, usually the constitutional disturbance is not severe, and the patient may escape careful abdominal examination until the symptoms of complete obstruction have appeared.

SUMMARY

Four cases of intussusception from eight to sixteen days' duration are presented, three of which were ileocecal and one of colonic invagination. The first three occurred in infants from 6 to 8 months of age, and the fourth in a boy aged 8 years.

The three infants had been nursed from birth, and except for slight digestive disturbances had never been ill. At the onset of the present illness the three infants had bloody stools, varying from a few tablespoonfuls in two cases, to enough to constitute a profuse hemorrhage in the third case. There was vomiting and pain at this time and subsequently the stools became watery. On physical examination, in two of the patients, a tumor was found in the right and left lower quadrant, respectively, of the abdomen. Operation, performed on two of the patients eight days after onset, resulted favorably. The third case came to necropsy sixteen days after onset.

In the boy aged 8 years, no fresh blood had been noticed at any time in the stools. The colicky pain, vomiting and the tumor pointed to an invagination of the bowel. Operation, performed eight days after the first attack of pain and vomiting, resulted in his complete recovery.

SO-CALLED IDIOPATHIC CARDIAC HYPERTROPHY IN INFANCY *

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Marked hypertrophy of the heart in infants and young children, without sufficient anatomic changes at autopsy to explain the hypertrophy on the basis of ordinary pathologico-physiologic processes, has been reported in about twenty cases. Below is the report of a case that we wish to add to the series already recorded.

REPORT OF CASE

History.—D. M., a girl, white, aged 10 months, was admitted to Bryn Mawr Hospital, June 14, 1922. The family history was negative. The father and mother, each in the thirties, were physically healthy. Five other children were living and well. There had been no miscarriages. The patient had been breast fed for less than six months; she had always been puny, but never edematous. Nothing was known about infections.

Present Illness.—Until a few days before admission the patient seemed to be in a normal condition. She then became sick and feverish, with a temperature of 102, pulse 140, and respiration 50. On admission, percussion of the whole left chest gave a flat note. There were many râles on the left side posteriorly. The heart sounds were normal. A diagnosis of pneumonia was made. The temperature returned to normal within four days of admission, and the patient seemed fairly well. The percussion note continued permanently flat over the whole left chest. Roentgen-ray examination showed a greatly enlarged heart. The pulse rate dropped with the temperature from 140 to 110, but never fell below this level. Respirations continued from 30 to 50 until the terminal illness.

Physical Examination.—On August, 10, the weight was 15 pounds 10 ounces (7.087 gm.). The measurements were: length, 70 cm.; head, 44 cm.; chest, 44 cm.; abdomen, 42 cm. The anterior fontanel admitted one and one-half fingers. The eyes reacted to light. The glandular system showed no enlargements. The liver and spleen were palpable. The chest was asymmetrical, bulging over the cardiac area. The left hemithorax measured 1 cm. more than the right at the level of the apex beat. The relative cardiac dulness was percussed into the axilla on the left and on the right extended 1.5 cm. from the midsternal line. The heart sounds were well heard and essentially normal. There were no thrills. The second aortic was greater than the second pulmonic. The lungs were practically clear to percussion and auscultation, except that the breath sounds were diminished over the left chest.

The diagnosis was idiopathic cardiac hypertrophy (so-called).

Course in Hospital.—On account of the persistent flatness in the left chest, on July 20 a needle had been inserted in the mid-axillary line without result. It probably entered the compressed lung and the persistent flatness was pre-

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* Received for publication, Feb. 12, 1924.

* From the Byrn Mawr Hospital and the Laboratory of Postmortem Pathology of the Philadelphia General Hospital.

sumably due to the greatly enlarged heart. The patient's condition continued good until a few days before death, when she developed signs of bronchopneumonia that terminated fatally, Aug. 31, 1922.

Necropsy.—A fairly well-nourished white female infant was seen, about 1 year of age. On opening the thoracic cavity the heart appeared to occupy the whole left side of the chest. The left lung was compressed and showed a few areas of congestion.

Heart: The pericardial cavity contained a small amount of bloody fluid with some fibrin but no adhesions. The heart itself was quite large and rather rounded. The hypertrophy was more to the left than to the right. The pericardium was smooth and glistening, except for a milk patch 1 cm. in diameter near the apex. The subpericardial fat was normal. The diameters were: transverse, 8 cm.; anteroposterior, 5.6 cm.; apex to origin of pulmonic artery, 7.5 cm. Circumference of valves: tricuspid, 6.4 cm.; mitral, 5.8 cm.; aortic, 3.5 cm.; pulmonic, 3.8 cm. Aorta, 3.4 cm. The wall of the left ventricle was from 1 to 1.2 cm., of the right ventricle from 0.4 to 0.6 cm. The weight of the heart was 136 gm.

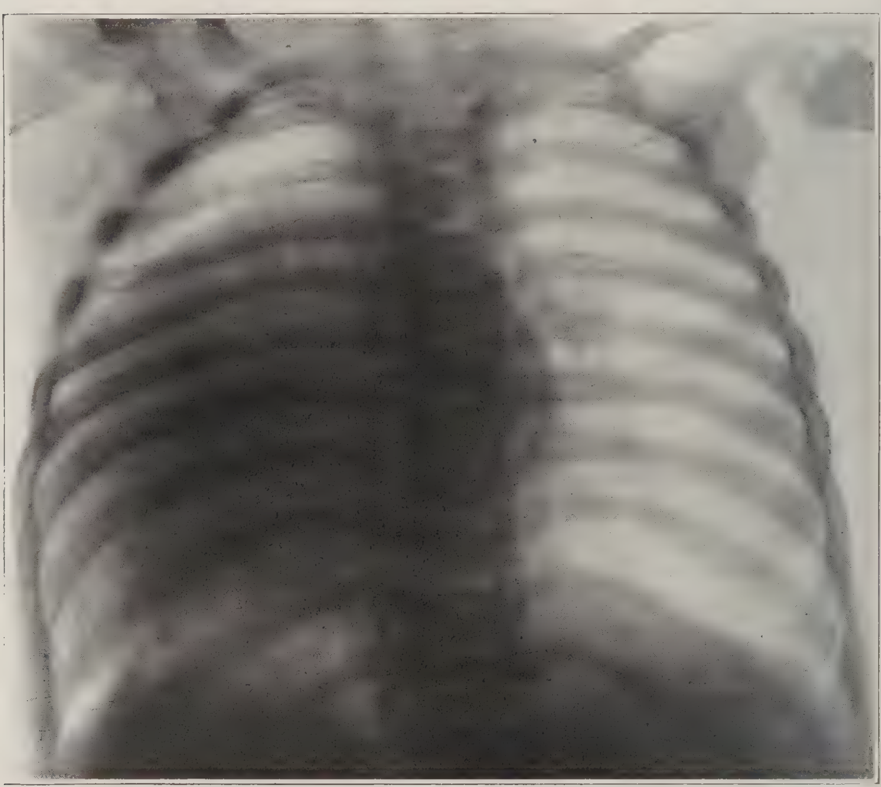

Fig. 1.—Posterior view of thorax of child showing idiopathic cardiac hypertrophy.

The right auricle and ventricle were a little hypertrophied but not dilated. The left auricle was both hypertrophied and dilated, and the endocardium uniformly thick and opaque. The chief change was in the left ventricle, which was greatly hypertrophied and dilated and its endocardium was slightly thickened in the basal portion. A trabeculation was marked and the mural endocardium of the septum was somewhat thickened. A thin abnormal tendon fiber joined the two papillary muscles. Easily detached red and gray thrombi nestled in the trabeculae near the septum. The anterior papillary muscle (normally supplied by the left coronary artery) was streaked with lines, apparently of fibrosis. The valves were all thin and delicate and appeared competent. The ductus arteriosus and foramen ovale were closed. No difference between the parts of the ventricles supplied by the two coronary arteries was observed grossly.

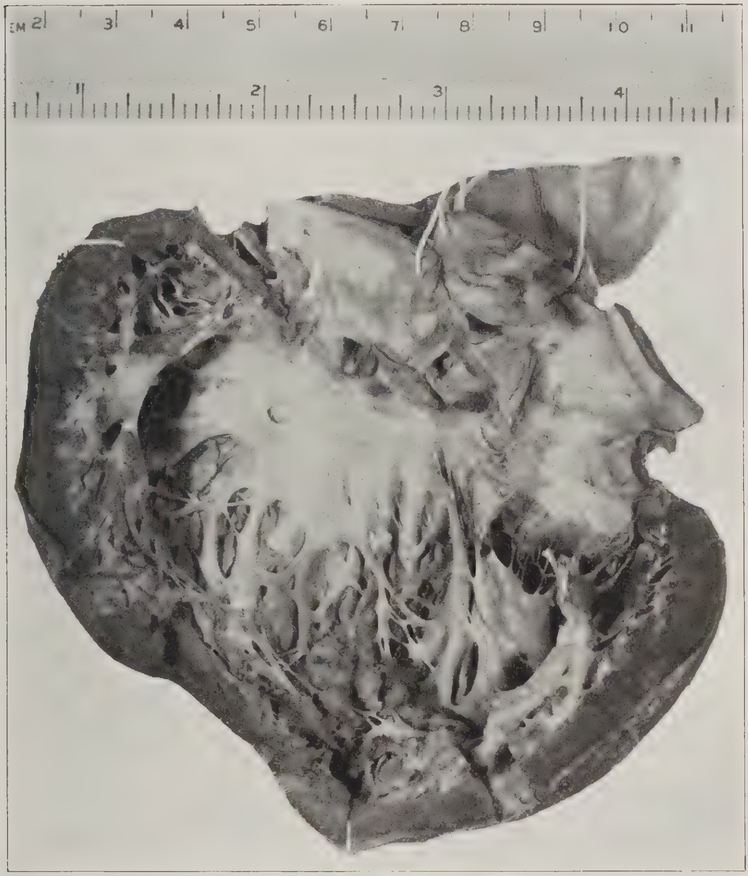

Fig. 2.—Left ventricle (weight of heart, 136 gm.) of 12 months old infant with idiopathic cardiac hypertrophy.

The left coronary artery arose anomalously from the pulmonary artery just above the posterior cusp. It divided after about 2 cm., the horizontal branch being much the smaller and only traceable for another 2 cm. The more important descending branch was lost a few centimeters before the apex was reached. Although the exact area supplied could not be determined in the absence of injections it was clear that the anomalous artery nourished much less than one half of the heart. It was estimated that it supplied the anterior portion of the septum, a fringe of the anterior right ventricle and about one half of the left ventricle. This probably included all or part of the anterior papillary muscle of the mitral valve.

Lungs: The left lung was somewhat compressed, with some areas of matting and congestion. Weight: left lung, 68 gm.; right lung, 96 gm.

Thymus: No abnormality noted.

The liver weighed 384 gm. Otherwise there was nothing of note. The gallbladder measured 2½ by 1 inch. The walls were thickened. The stomach and intestines were normal in appearance. The spleen and kidneys showed no gross abnormality.

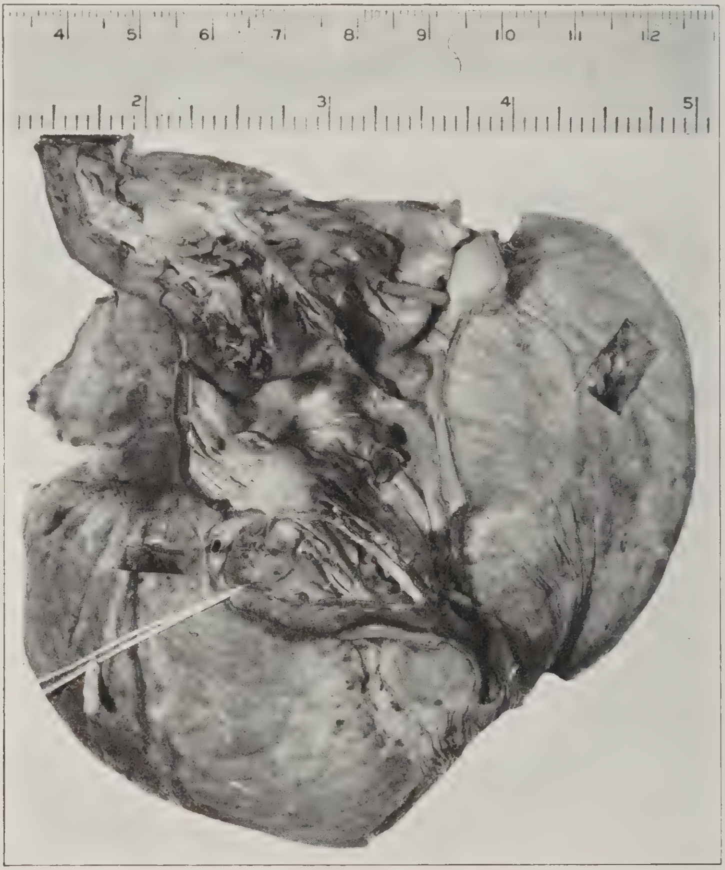

Fig. 3.—Right ventricle showing rod in anomalous coronary artery arising from pulmonary artery.

Anatomic Diagnosis.—Idiopathic cardiac hypertrophy, anomaly of coronary artery; bronchopneumonia (terminal).

Histology.—The heart: Sections from various parts of the ventricles showed large fibers, with a tendency to large rectangular nuclei. Many, however, were unduly wavy and separated by a slight amount of fleecy fibrous tissue. They had undergone considerable vacuolar degeneration. There was no increase in pigmentation or fragmentation. There was distinct increase of old interstitial fibrous tissue in sections from the anterior papillary muscle of the mitral valve and from the anterior portion of the septum. This was diffuse, rather than perivascular and nearer the endocardium than the pericardium. The parenchymatous degeneration (loss of striae and vacuolization) was also most marked in the areas supplied by the anomalous artery. There were no abnormalities in the coronary vessel walls. The diagnosis was parenchymatous degeneration of myocardium and slight, localized myocardial fibrosis.

The lungs: Conglomerate areas of bronchopneumonia; alveoli filled with polymorphonuclear cells (many degenerated) also large mononuclear cells and débris; the bronchi were also full of polymorphonuclears. In other areas, heart failure cells and fleecy pink staining material predominated. The diagnosis was bronchopneumonia and edema.

Liver: The strands were more separated than usual and many liver cells had a fleecy, somewhat shredded appearance. The diagnosis was slight passive congestion; cloudy swelling.

In the kidney there were distinct but moderate inflammatory changes in the cortex and medulla. In some areas small round cells replaced the tubules partly or completely, and some of the latter were dilated and contained casts. Numerous vessels were congested. A few glomeruli were shrunken or wholly converted into fibrous tissue, or contained thrombi. The convoluted tubules were much swollen. The diagnosis was chronic mixed nephritis (slight).

COMMENT

It will be noted that there was no urine examination made, and that microscopically the kidneys showed definite pathologic changes. While we do not believe that the renal damage is an important etiologic factor in these cases, we are not prepared to go so far as Howland [1] when he says that nephritis can be dismissed from consideration as a causative factor; especially since in the five cases reported by him there was not one where the study of the kidney was complete and normal. Of the five cases urine examinations were not reported in three cases, one case had albumin, and the fifth had albumin, white and red blood cells. The kidneys in two cases showed gross pathologic changes and in these two no histologic report was included. Yet the cardiac hypertrophy in all of these has been so tremendous, and the pathologic findings elsewhere so meager, that we can hardly conceive of an explanation on the basis of the ordinary pathologico-physiologic processes of nephritis.

More important in the present case is the anomalous origin of the left coronary artery from the pulmonary artery. The nourishment of a considerable part of the cardiac musculature with venous blood cannot be without significance, and yet here the hypertrophy of the myocardium apparently occurs regardless of its source of nourishment, and the degenerative changes of the anomalously supplied muscle seem to be insufficient causes for the tremendous hypertrophy.

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[1] Howland, J.: Idiopathic Hypertrophy of the Heart in Young Children, in Contributions to Medical and Biological Research, Dedicated to Sir William Osler, in Honor of His Seventieth Birthday, July 12, 1919, by his pupils and co-workers, Johns Hopkins Press, 1919.

The explanations offered for this condition by various writers at different times have been: (1) Enlarged thymus; (2) prolonged pertussis or pulmonary disease such as atelectasis or pneumonia; (3) congenital malformation of heart or great vessels; (4) marked rickets of the thorax; (5) diffuse rhabdomyoma of heart (Virchow[2]); (6) a chemical stimulus in the blood; (7) excessive stimulation from the chromaffine system (Hedinger[3]); (8) dilation and hypertrophy following lack of sufficient secretion of the chromaffine system (Michaud[4]); (9) some disturbance of the intra-uterine circulation.

Any comment on these suggested causes in this case would be purely speculative in the present state of our knowledge, and would add nothing of value. There are a few facts, however, that are worth noting about the condition: (1) it is at least sometimes congenital, as two cases have been reported in stillborn infants; (2) some patients have not shown symptoms until they were from 2½ to 4½ years of age, which would make a late hypertrophy seem possible; (3) the break in compensation is surprisingly disastrous, considering the fact that there is hypertrophy without marked or extensive degeneration of the heart muscle fibers; (4) it is not established whether the increase in the size of the heart is due to hypertrophy of the existing fibers, hyperplasia, or both; (5) such factors as slight nephritis and anomalous origin of a coronary artery, as in the present case, are not considered adequate causative factors; (6) the condition would appear to be not especially rare, as evidenced by Oberndorfer's[5] having seen five cases in one year. Congenital rhabdomyoma of the heart is such a different affair that it need not be considered further here.[6]

It is interesting to note that in the case we report there were evidences both of a moderate nephritis and of pulmonary disease. The renal changes though of unknown origin, were thought to be of relatively short duration and not to have played an important part in the cardiac hypertrophy. The rôle of the anomalous coronary and the slight myocardial fibrosis, though unimportant, must still be considered. The pneumonic signs that were present on admission were probably due to a mild infection occurring in an area of the lung that had been compressed by the enlarged heart, rather than the pulmonary infection being an important factor in the cardiac hypertrophy. The signs of a terminal bronchopneumonia were found at necropsy. Certainly none of these factors would ordinarily account for the hypertrophy of the heart from a normal size of from 35 to 40 gm. (Vierordt[7]) at the age of 12 months to the weight of 136 gm. found in this patient.

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2. Virchow: Berl. klin. Wchnschr. **33**:679, 1896.
3. Hedinger: Cor. Bl. f. schweiz. Aerzte **35**:260, 1905.
4. Michaud: Cor. Bl. f. schweiz. Aerzte **36**:779, 1906.
5. Oberndorfer: Verhandl. d. Gesellsch. f. Kinder. 1906, p. 181.
6. Schmincke: Beitr. z. path. Anat. u. z. allg. Path. **70**:513, 1922.
7. Vierordt: Daten und Tabellen für Mediziner, 1906, p. 36, 37.

Howland's article brought the subject up to date in 1919, but is rather difficult of access. Since that time we have been unable to find any new contribution to the subject.

SUMMARY

1. A case of so-called idiopathic cardiac hypertrophy is reported in an infant aged 12 months.

2. A mild nephritis, myocardial fibrosis and anomalous coronary artery (arising from the pulmonary) are discussed as possible causes.

3. It is probable that this condition includes hypertrophies due to various antenatal and postnatal factors, some of which are still unrecognized, and is seldom, if ever, truly idiopathic.

TUBERCULOUS PYOPNEUMOTHORAX IN AN INFANT AGED FIVE MONTHS *

S. G. ROSS, M.D., AND C. T. CROWDY, M.D.

MONTREAL

Pneumothorax as a complication of tuberculosis in infancy is apparently an uncommon condition. This is the opinion of all writers on the subject. Bourne [1] has recently reported a case in which the condition developed in an infant, aged 18 months. To our knowledge this is the youngest patient in whom this complication has been reported. For other reasons, subsequently presented, the case is also noteworthy.

REPORT OF CASE

R. M., a boy, aged 3 months, was admitted to the Pediatric Department of the Royal Victoria Hospital, Jan. 22, 1923, suffering from cough and loss of weight.

Family History.—The patient's father was suffering from advanced pulmonary tuberculosis and living at home with his family. The mother was in poor health but showed no evidence of active tuberculosis. There had been six pregnancies. The first four children died respectively of diarrhea, meningitis, diphtheria and influenza between the ages of 5 months and 3½ years. The family lived in very poor and cramped quarters.

History.—The patient at birth weighed 5½ pounds (2,495 gm.), and appeared healthy. He was breast fed for one month. After that he was fed on proprietary foods and cow's milk dilutions. There were no digestive disturbances.

Present Illness.—The infant "caught cold" two weeks before admission. Since then he had a cough of moderate severity, and had lost weight and vomited occasionally.

Examination.—A well developed and fairly well nourished infant was seen, weighing 8 pounds, 7 ounces (3.9 kg.). He was slightly pale. There was no superficial glandular enlargement. The temperature was 98, pulse 110, respirations 36; the length of the patient was 52 cm.; circumference of the head 35 cm.; of the abdomen, 33 cm.; of the chest, 33 cm. The ear drums were normal. The chest was symmetrical, and the lungs resonant throughout. On auscultation, breath sounds of the normal puerile character were heard. A few large moist râles were heard, which cleared up on coughing. The heart and abdomen were normal. The urine was also negative. Hemoglobin, 70 per cent. White blood count, 16,000; red blood count, 3,600,000.

Course of Disease.—January 25, an intradermal tuberculin test, $\frac{1}{10}$ mg., showed a doubtful positive reaction.

January 30, the child did fairly well since admission, and took his feedings well. He had a slight cough.

January 31, the temperature rose to 100 the previous day. Examination of ears showed left otitis media.

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* Received for publication, Feb. 27, 1924.

* From the Department of Pediatrics, Royal Victoria Hospital, and the Pathological Institute of McGill University.

[1] Bourne, G.: Brit. M. J. **1**:526 (April 9) 1921.

February 1, the temperature was 101.3. Double otitis media had developed. Paracentesis of both ear drums was done. The patient also had moderate diarrhea.

February 3, the temperature fell to normal. Both ears were discharging freely, and the patient was losing weight.

February 6, a few medium moist râles were heard in the right axilla. There was profuse aural discharge.

February 7, an injection of intradermal tuberculin, $\frac{1}{10}$ mg., showed a definitely positive reaction. The spleen was palpable. Roentgen ray of the chest (Fig. 1) showed a slightly increased density at the root of the right lung and a patch of increased density in the lower part of the left lung. This patch was probably due to a tubercular focus.

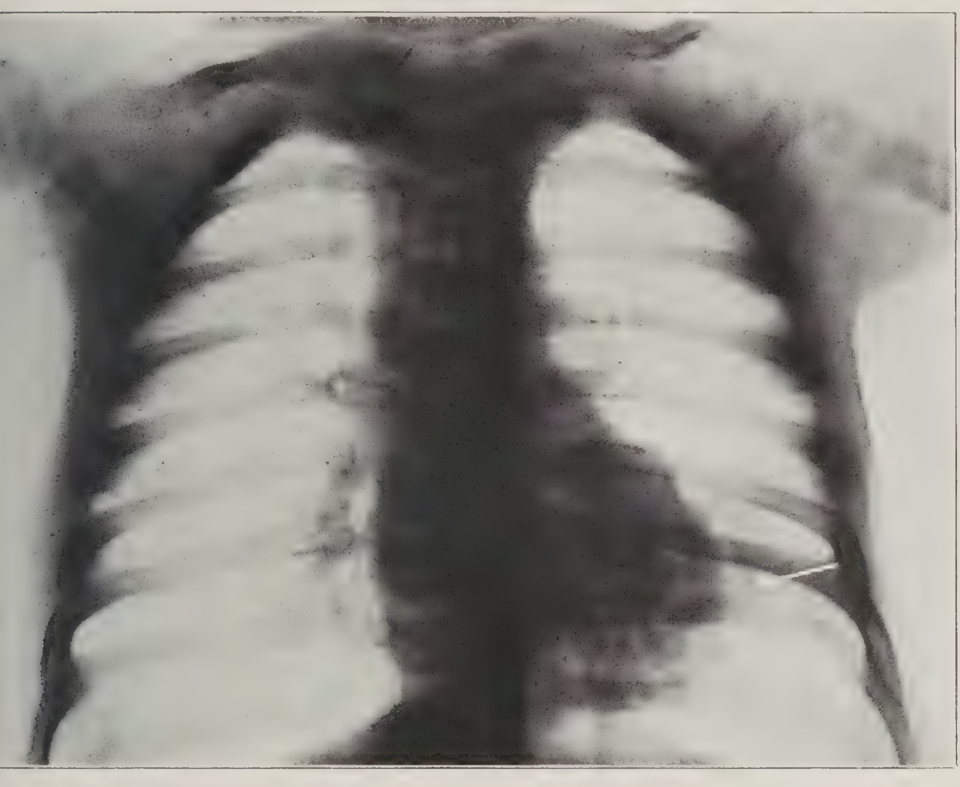

Fig. 1.—Increased density at the root of the right lung, and increased density also in the lower part of the left lung (see arrow).

On account of an outbreak of chickenpox in the ward, the patient was discharged. The diagnosis at that time was: (1) Tuberculosis of tracheobronchial lymph nodes; and (2) bilateral suppurative otitis media. It was suspected that there was probably also a primary focus of tuberculosis in the left lung as demonstrated by the roentgen ray. The patient developed varicella ten days after discharge, from which he made a good recovery.

Second Admission.—The patient was admitted to hospital again on April 10, aged 5 months. The cough had persisted during his stay at home and during the week previous to admission had become worse. His weight had remained stationary.

Examination.—The length was now 54 cm; circumference of the head, 37 cm.; of the chest, 34 cm.; of the abdomen, 34 cm. and his weight 8 pounds (3.6 kg.). The temperature was 97, pulse 100 and respirations 30.

The patient was poorly developed and undernourished and appeared ill. His color was pale, with a grayish tinge to the skin. There was slight cyanosis. The skin exhibited scars of recent varicella. There was a definite loss of subcutaneous tissues. No superficial glandular enlargement was noted. The head and eyes were normal. The left ear drum was gray and opaque; it did not bulge, but showed the scar of the old perforation. The right ear drum was gray and opaque, with a small perforation in the posterior half. There was no discharge. The lips were pale and slightly cyanosed. The mouth was normal. The chest was symmetrical. Both sides moved equally on respiration. The percussion note of the lungs was normal throughout. The breath sounds were bronchovesicular in character. In the left upper lobe and high in the left axilla a few fine crepitations were heard. An occasional moist râle was heard in the right lung. The heart was normal. The abdomen rounded, with the liver palpable one finger's breadth below the costal margin. The spleen was palpable. The muscles were weak and of poor tone. The nervous system was normal. The urine was negative. White blood count, 14,000; red blood count, 4,100,000; hemoglobin, 65 per cent. The blood Wassermann was negative.

Course of Disease.—On the evening of admission the patient had a sudden attack of acute dyspnea, with violent coughing lasting several minutes. Examination showed the chest movement was extremely limited in respiration. On percussion the left side of the chest was definitely hyperresonant. The heart dulness was obliterated on the left side and the heart apparently pushed over to the right, the apex beat being felt just to the left of the sternum. Over the left side of the chest the breath sounds were distant and blowing in character. Over the left upper lobe numerous tinkling musical râles were heard. The characteristic coin sound was present. The diagnosis was pneumothorax of the left pleural cavity.

April 10, the general condition was poor, and the respiration was embarrassed. The pulse was 150. The left side of the chest was immobile and showed some bulging with still definite hyperresonance. The breath sounds were distant. The tinkling râles were no longer heard. The coin sound was present, but not so characteristic.

April 12, there was a slight rigidity of the head with a suggestion of Kernig's sign on the left side.

April 13, a discharge from right ear was noted. On auscultation of the chest fine crepitations were heard throughout the right lung.

April 14, the apex of the heart was felt in the midline just below the xiphisternum.

April 15, the patient coughed more. There was dulness on percussion at the left base suggesting fluid.

April 16, the patient appeared weaker. A specimen of sputum obtained from the throat showed the presence of acid-fast bacilli of the morphology of tubercle bacilli. The voice sounds at the lower angle of left scapula were of a distinctly amphoric quality.

April 17, lumbar puncture was attempted, but stopped on account of cyanosis and cessation of respiration.

April 18, an injection of $\frac{1}{10}$ mg. intradermal tuberculin was given, with a decided positive reaction. Dyspnea was more marked; the patient became very weak and died.

Necropsy.—A cisterna puncture was done immediately, and 5 c.c. of turbid fluid was obtained. In the cell count of 1,200, predominantly lymphocytes, no tubercle bacilli were found. The smear showed numerous gram positive lancet shaped diplococci of the morphology of pneumococci (definitely capsulated). The diagnosis was possibly a terminal pneumococcic meningitis. Throughout the last admission the temperature did not rise above normal. The weight increased from 8 pounds to 8 pounds 6 ounces (from 3.6 to 3.9 kg.)

Roentgen-Ray Reports.—April 11, showed pneumothorax in the left side and a small quantity of fluid in left side of the chest.

April 13 (Fig. 2) showed pneumothorax in the left side, with adhesion of the left lung to the region of the fifth rib at its lateral aspect. The upper part of the pneumothorax extended across to the right lung, reaching about 1 (2.5 cm.) inch beyond the middle line. The trachea and heart were very markedly displaced to the right. Little or no fluid was present. The left pleura showed definite thickening.

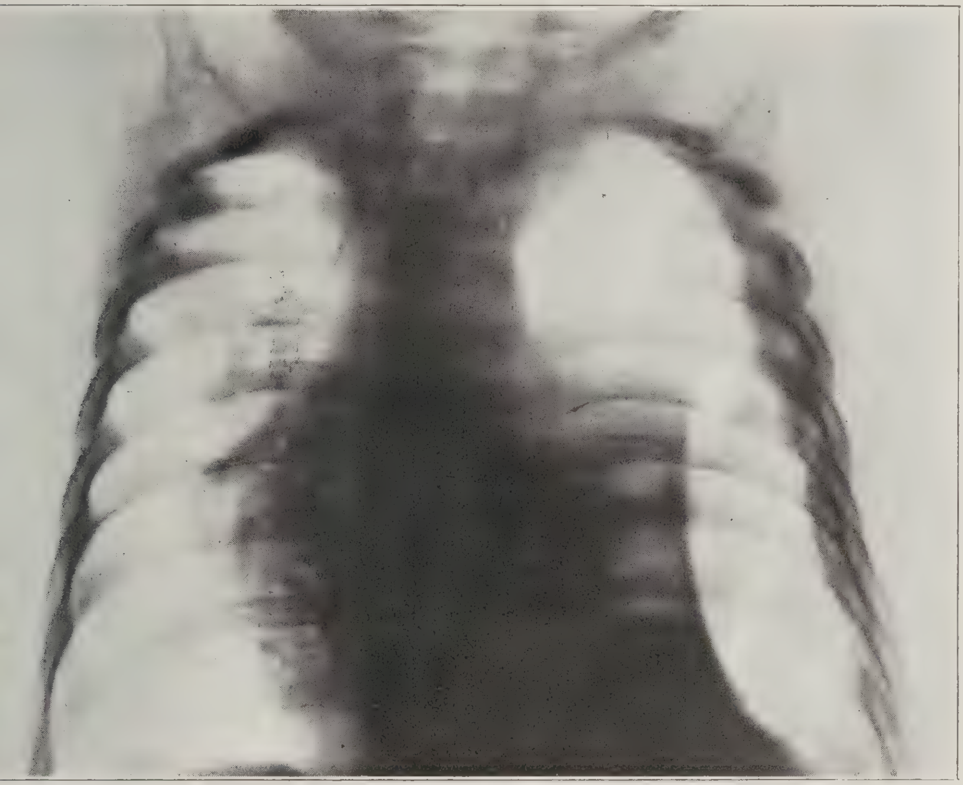

Fig. 2.—Pneumothorax of the left side with lung adhesion. The pneumothorax extends to the right lung.

Clinical Diagnosis. — (1) Pulmonary tuberculosis, (2) tuberculosis of tracheobronchial lymph nodes, (3) tuberculous pneumothorax, and (4) chronic suppurative otitis media.

NECROPSY REPORT OF DR. CROWDY

The chief interest at necropsy centered around the left thorax. Inspection disclosed this side was more prominent than the right. Puncture of the third intercostal space under water demonstrated the presence of air in the left pleural cavity. On opening the thorax, the right lung and heart were displaced to the right, the right lung was compressed and the pleural cavity contained 2 c.c. of serous fluid. The left lung was collapsed and compressed against the heart and spine, with complete obliteration of the mediastinal part of the pleural cavity and filled approximately only two-fifths of the left thorax. The remainder was represented by a cavity lined by a pyogenic membrane and filled posteriorly with thick, purulent fluid. The anterior part of the cavity was empty and contained air which escaped on puncture. The anterior border of the lung was adherent to the fifth, sixth and seventh ribs just external to the junctions of the corresponding cartilages. This drew the lung out at this point into a fold, and apparently divided the cavity into two parts (Fig. 2), but really only slightly constricting it at this point. The left lung was then removed with the mediastinal tissues, by dissection between the parietal pleura and the ribs. In this way the left thorax was kept intact. On removal, two perforations (Fig. 3) in the visceral pleura near the midlateral aspect were visible and these communicated with a pulmonary cavity.

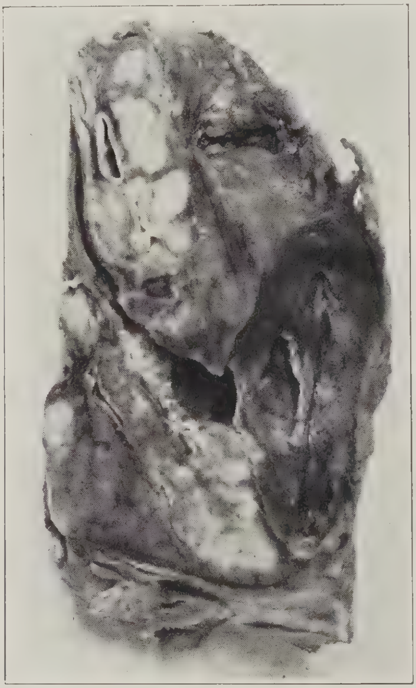

Fig. 3.—Perforations in the visceral pleura.

The specimen was preserved in Kaiserling's solution (No. 1) for several months, and in this way a perfect preservation of colors and tissues was obtained. Examination with a probe showed that a main branch of the bronchus communicated with the cavity and section was so planned as to open the trachea, left bronchus and the branch which opened into the pulmonary cavity (Fig. 4). The cut surface showed the following additional interesting points: In the first place, the lung was so compressed and diseased that the division of the upper and lower lobes was lost and the lung fused with the mediastinal tissues. Secondly, the mediastinal glands (Fig. 4) were enlarged, completely caseous and fused together by hyaline thickened capsules. The left pulmonary artery was surrounded and compressed by these glands so as to show only a slitlike opening. The central part of the lung showed advanced tuberculous pneumonia (caseation), and in the center of this was a triangular cavity measuring 2 by 3 cm. (Fig. 4) with its base at the pleural surface and its apex communicating with a bronchus (Fig. 4). The apex of the lung and a small triangular area at the base were atelectatic and showed only a few pin point caseous spots.

A brief description of the remaining organs will suffice. The right lung was free in the right thorax, which contained approximately 2 c.c. of serous fluid. The apex and anterior margin showed slight emphysema, but the lung as a whole was somewhat compressed. There were a number of small nodular masses which showed through the pleura as slightly raised yellow elevations which varied in diameter from 1 to 5 mm. On section, these nodules were caseous throughout and the center of the upper lobe showed more recent miliary conglomerates.

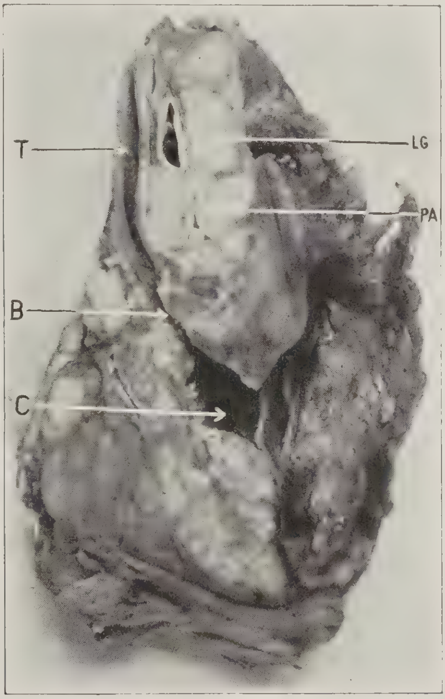

Fig. 4.—Direct communication of trachea (*T*) with cavity (*C*). Caseous and fused mediastinal lymph glands (*LG*). Compressed left pulmonary artery (*PA*). Point at which microscopic section taken (*B*).

The brain showed no microscopic tubercles, but the meninges were edematous at the base and were gelatinous. The peritoneum and abdominal organs were without gross lesions. The intestine and mesenteric lymph glands were very carefully examined for a possible primary focus, but no evidences of any infection were discovered.

The microscopic lesions were very typical and of especial interest as they bear on the probable sequence of events. The mediastinal glands revealed complete replacement by cheesy caseous material and fused with the surrounding hyaline fibrous tissues. A section, taken through the bronchus leading to the cavity and the surrounding tissue at the pointed marked B (Fig. 4) showed a well marked proliferation and desquamation of the lining epithelium of the bronchus with exuded serum and mononuclear cells. The submucosa was very vascular and infiltrated with similar inflammatory cells. The epithelium of the bronchial glands showed disintegration. In close proximity to the bronchus were two small peribronchial lymph glands. These showed central caseation surrounded by an epithelioid celled zone and giant cells, but separated from the bronchus and each other by granulation tissue, rich in large pale mononuclear cells.

Sections of the brain through the sylvian fissure and middle cerebral artery showed a very marked lymphocytic infiltration following the course of the vessel. There was however, no fixed tissue reaction either in the form of endothelial proliferation or formation of definite tubercles.

In the liver and spleen were scattered minute tubercles consisting of epithelioid cells and an occasional giant cell, without caseation.

COMMENT

In reviewing this case from the clinical standpoint, several facts stand out in bold relief. The close association with the father, who was suffering from open tuberculosis, was the evident reason for the early infection of the patient. As to the mode of entry of infection one cannot dogmatize. However, the necropsy findings showed no evidence of tuberculosis of the alimentary tract. In this connection the possibility of infection by this route, with passage into the lymphatics and general circulation without causing a local lesion, must be considered. Another possibility is that the otitis media was of a tuberculous nature. There is no proof for or against this. The obvious and, therefore, attractive theory is that inhalation of droplets or dust carrying the tubercle bacilli resulted in a tracheobronchial lymph node infection by way of the pulmonary road. In favor of this is the history of a persistent cough from the age of 3 months, and the presence of shadows at the hilum in the roentgen ray. These at such an early age are suggestive of tuberculosis. Finally, and what seems of most importance, a definite shadow (Fig. 1) in the middle part of the left lung, which later was proved to be the center of the tuberculous lesion.

As to the diagnosis, we would like to emphasize the importance of the history of exposure, which should always lead one to search carefully for signs of tuberculosis. When first seen, it was impossible to make a diagnosis by physical examination alone. Here the obvious value of the tuberculin test and the roentgen-ray examination is apparent. The first tuberculin test was doubtful, but on being repeated gave a definitely positive reaction. The intradermal method was used, being much more reliable than the Pirquet cutaneous method. A positive test at this age always means active tuberculosis. The roentgenogram of the chest showed definite signs of enlarged glands at the hilum and of parenchymal consolidation as well. This, in the presence of a positive tuberculin reaction, made the diagnosis quite certain. Without these two aids the diagnosis would have been impossible until much later in the course of the disease.

The prognosis in tuberculosis when infection has taken place in the first three months is practically always fatal, and either a miliary tuberculosis, a tuberculous meningitis, or more rarely a tuberculous bronchopneumonia may follow the original infection.

It was possible by the roentgen ray to diagnose the anatomic lesion of the lungs with great accuracy. The tuberculous adhesions attaching the lung to the parietal pleura and preventing complete collapse of the lung are well shown and, as previously noted, were confirmed at necropsy. It would also appear that the portion of the lung, which showed the first sign of disease by the roentgen ray, was the place at which the caseous mass broke through into the pleural cavity. The roentgen ray also showed a definite thickening of the left pleura which was confirmed at necropsy.

It is of interest to note that during the last illness of the patient there was no fever. This may occur in overwhelming infections with tuberculosis.

The pathologic findings, both gross and microscopic, confirm the clinical in nearly every respect. It seems to us that all the evidence points to the following sequence of events: Infection of the respiratory tract by direct contact, passing of the bacilli into lymph channels and spaces of the peritracheal or peribronchial tissues and involvement of the peribronchial and peritracheal lymph glands. The complete destruction of these glands and the degree of caseation point to these as the oldest lesions in the thorax. In the absence of any anatomic evidence in the intestine or mesenteric lymph glands, it would seem permissible to question seriously or even rule out the intestinal route.

It would seem that there is probably a relation between the marked involvement of the greater part of the central portion of the left lung and the compression of the main branches of the pulmonary artery (Fig. 4), which supply this area. There are two possibilities, either a direct invasion of the wall of one of the branches of the artery or a rupture into a corresponding bronchus. Either event would throw bacilli into a part of the lung in which the resistance was lowered by interference with the circulation. That the lung lesion was at first localized to such an area is, we think, well shown by the roentgenogram (Fig. 2). Then followed caseation with extension of the lesion and cavity formation. The direct connection of the cavity with a larger bronchus allowed aspiration of infected material into the right lung. The very recent lesions in the meninges, liver and spleen may be considered due to a terminal invasion of the greater circulation.

HEALTH AND GROWTH OF CHILDREN IN AN INSTITUTION *

S. E. KATZ, M.S., AND HORACE GRAY, M.D.
BOSTON

"Children in an institution can be kept in much better condition than in most private homes."[1] This contradiction to the prevalent impression, and tribute to institutional possibilities, has been illuminating to us, as we have been engaged for six months in a somewhat similar study. This study differs in certain particulars, which will be recited below, but mainly in two: (1) It concerns children of the very poorest classes, namely, of parents who were either unable to support them, or who were dead, and (2) it investigates not only the physical status, but also the anthropologic and mental. The present paper in a large degree confirms Holt and Fales'[1] surprising but important findings, and considers certain further points of interest in connection with institutional children.

THE INSTITUTION

The institution is a Home for Jewish Children, receiving them from a child caring agency. The house is a brick building of three stories, with plenty of air space and ventilation. Its situation is in a big Jewish community on an elevation at the outskirts of Boston, facing a park. There is a dormitory for each of the following four groups, older and younger boys, older and younger girls. These dormitories are located on the second and third stories with bathing facilities adjacent; the dining room and offices are on the ground floor; and in the basement are shower baths and wash basins which the children use after play hours. The playground consists of a big yard in the rear of the building enclosed by a high brick wall, and is furnished with an adequate amount of apparatus of which the children make frequent use. During the summer months, the older children are usually sent for a fortnight to the country, where a camp is maintained by the institution.

INMATES

Contrary to Holt and Fales' subjects, practically all of these children come from the very poorest class; most of them are orphans, some half orphans, only a few have both parents. The race is, of course, Jewish. Nearly all are native born, while their parents were

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* Received for publication, Jan. 23, 1924.

[1] Holt, L. E., and Fales, H. L.: Observations on the Health and Growth of Children in an Institution, Am. J. Dis. Child. **26**:1 (July) 1923.

practically all foreign born. Most of the children have been raised in the city. At first observation the children appear to be in good physical condition, with very few exceptions, and furthermore, happy and gay, not suffering in the least from institutional repression.

The ages of the children range from 5 to 17 years, though there are very few below the age of 6 or above the age of 16.

The length of stay, as one would naturally expect for children of this destitute class, is rather long. The girls show a longer residence than the boys. The average is 4.3 years. The mode (commonest stay) corresponds. Twenty-five per cent. have been in the institution for five years, or more, and only a very small percentage have a residence of less than one year (Table 1).

TABLE 1.—*Years of Residence*

	Less Than 1 Yr.	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	Totals
Boys, number..........	14	14	17	12	20	6	6	4	3	1	0	0	97
Girls, number..........	6	8	9	10	7	4	5	3	0	3	3	1	59
Both sexes, number.....	20	22	26	22	27	10	11	7	3	4	3	1	156
Percentage.............	13	14	17	14	17	6	7	4	2	3	3	0.8	98.8

The number of families represented in the institution was eighty-one. The size of family from which the children came is shown in Table 2. The mode is 4, the average 4.6 children. This point is of interest because it shows that the families are smaller than is usually believed to be the case in this class.

TABLE 2.—*Size of Family*

	Number of Children in Family										Not Ascertained	Total
	1	2	3	4	5	6	7	8	9	10		
No. of instances of each....	4	9	26	37	26	17	13	8	0	2	14	156

The distribution of siblings actually in the institution is seen in Table 3. The mode is one and the average is 1.93.

TABLE 3.—*Distribution of Siblings*

	Number of Siblings						Total
	1	2	3	4	5	6	
Number of such instances......................	37	22	16	4	1	1	156

GENERAL HEALTH

On application for admission, a complete physical and mental examination is usually given by the physician of the child caring agency, to exclude children who are defective or acutely ill. Malnutrition, however, is not a cause for exclusion, but rather for admission. There is no quarantine regulation for children admitted. The institution has a small hospital, where children who become ill are separated and cared for by the resident nurse. She also attends to all minor ailments or slight injuries. The more serious ones are seen by the visiting physician who gives the children a general physical examination once a year. No epidemic of any sort has occurred for a number of years, and deaths are rare. During the last year there were few cases of serious illness; any such case is immediately removed to one of the city hospitals.

The good health of the children is probably the result of the regular life. The prevalent impression that children living in an institution decline in vitality, and that their development is inhibited, would be greatly modified by visiting an institution of this sort. Observation of these children would lead to the belief that institutional life may just as well accelerate growth. As Holt and Fales state: "The carefully controlled life in any properly managed institution, the regular hours, the good food and the lessened chances of infection, make it possible to keep children in institutions in excellent health, in fact in much better condition than they could be kept in most private homes," especially where the sanitary conditions in the Ghettos of the big Jewish centers in the East leave much to be desired. Except at the public school, our children do not come in contact with others.

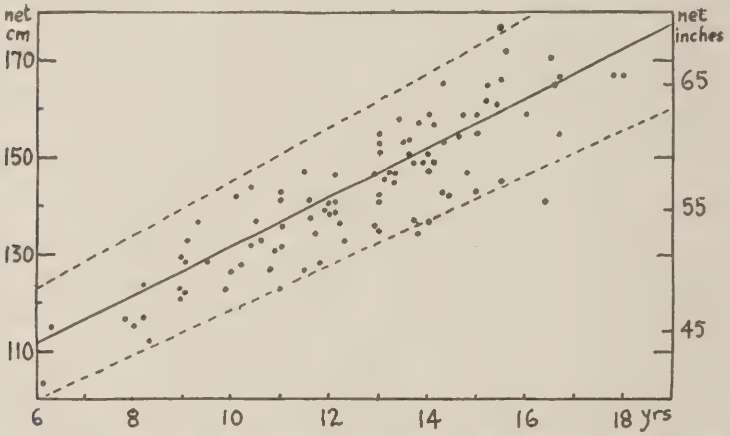

Chart 1.—Height for age, boys. The solid line in each chart shows the standard height, and the dotted line shows the zone 10 per cent. below and above the standard height.

ROUTINE

The regimen, although strict, is liberal enough not to interfere with the activity of normal children. They rise at 6 a. m., have about a half hour to attend to their toilet, and then attend a short service.

At 7 they have breakfast. In the dining room they have more liberty than in many institutions; they are allowed to talk and even to move about somewhat. A prayer is offered at the beginning and the end of each meal, and for a few seconds before the prayer, no talking is allowed. About thirty minutes are given to each meal.

After breakfast the children make up their own beds. From 9 a. m. to 12 m. they attend the neighboring public school. At 12:30 dinner is served, after which they return to school for a while. At the Home again at 3 p. m. the older boys have manual training (printing, carpentry, machine work) and the girls domestic science. Both also have Hebrew classes. The younger children have this time for play. No systematic physical education is provided at present. Supper is served at 5:30 p. m. Evenings are spent partly in studies, somewhat supervised, and partly at play. The younger children go to bed at 7 p. m., the older ones at 9. Children must take showers at least twice a week. Special emphasis is laid on oral hygiene, tooth brush and paste being expected to be used twice a day.

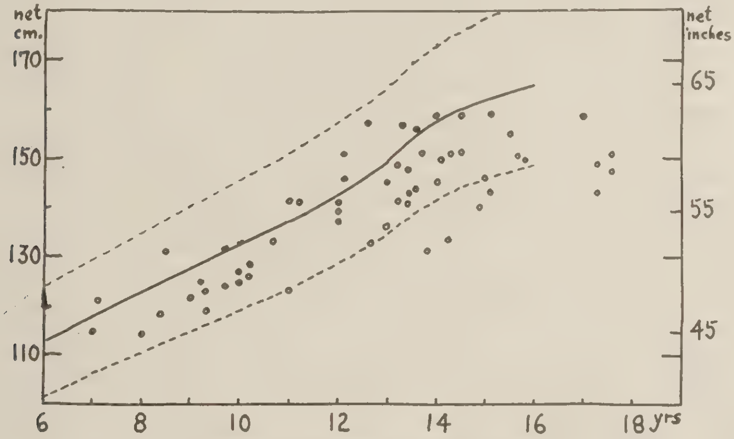

Chart 2.—Height for age, girls.

During July and August the rising hour is changed to 7 a. m., and breakfast is at 8. The morning period from 9 to 12 is spent at manual training or Hebrew classes, the afternoons and evenings are given over to play. At frequent intervals the children are taken out to the beaches or other places for recreation.

The institution takes special pride in its Boy Scouts and Camp Fire Girls, to which the older children belong. The summer camp is conducted by these organizations. The children are also encouraged to participate in various sports. They have a basketball team in the winter and a baseball team in the summer time. Competition for membership on these teams is keen.

DIET

The meals are plentiful and consist of the food usually served in Jewish homes. Breakfast consists of cereal, fruit, cocoa and bread and butter; dinner consists of soup, meat and a vegetable, bread, some sort of pudding and water; supper consists of milk soup, jelly and bread and butter with either cooked or uncooked fruit as dessert. Eggs and fish are often substituted for soup.

The food is served on big platters, one platter for a table. At the head of the table sits an older child who serves the five or eight children at his table. No attempt has been made to determine the caloric consumption, as this was impractical under the present dining room arrangement. The general appearance of the children is a sufficient index of the quality and quantity of the food consumed.

OBSERVATIONS ON GROWTH

As stated before, this report deals only with one phase of the investigation, namely, physical development. The subjects numbered ninety-seven boys and fifty-nine girls. Measurements were recorded in metric units. The weights were taken on a Fairbanks scale that had been checked before using. The scale reads to ¼ of a pound, and the readings were computed to tenths of kilograms. Shoes, coats, and contents of pockets were removed. The clothing (July) we found, like Holt and Fales, to average only 0.7 kg. (about 1½ pounds) while for the younger boys and girls it weighed somewhat less. Deductions have been made so that all measurements here reported are net. All the weighing was done between 10 and 12 in the morning; that is, from two to four hours after eating.

The height was taken as follows: The children removed their shoes and stood with head, heels and sacrum snugly against the wall. A light triangular piece of cardboard was brought down until it touched the vertex firmly, and the reading was then taken to the nearest millimeter. It was found that the error of two successive measurements was not greater than 2 mm.; this was owing to a change in position that a child may assume, and was found to be still further reducible by taking the measurements quickly. Stem length was also measured.[2] It is planned to take these measurements once a month to determine rate of growth and seasonal variations. The present paper deals only with the data found during the month of July at our first series of observations. These data have been analyzed for the relation of weight to height and height to age, relation of nutrition to birth, length of residence, size of family, tuberculous history of parents.

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[2] Gray, Horace: Sitting-Height and Stem-Length in Private School Boys, Am. J. Dis. Child. **23**:406 (May) 1922.

TABLE 4.—*Developmental Status—Relation of Height and Age*

	Percentage of Population			
	Above Average	1-10% Below Average	11% or more Below Average	Total
Boys	37	60	3	100
Girls	20	65	15	100
Both sexes	31	61	8	100

Age and Height Relation.—We noticed that the children were of rather low stature, for they exhibited a larger percentage of below average in height than the children studied by Holt and Fales.[1] This may be owing to either their racial difference or to the poorer economic status. Charts 1 and 2 show the height and age relationship in graph form. The solid line shows the standard height for age and is based on the values given by Holt and Howland.[3] The dotted lines in each chart mark the zone, including the height of boys and girls respectively, 10 per cent. below and 10 per cent. above the standard height for age (nearest birthday) as in Holt and Fales' article.

TABLE 5.—*The State of Nutrition, with Relation of Weight to Height*

	Percentage of Population			
	Above Average	Tolerable, i. e., 1-10% Below Average	11% or more Below Average	Total
Boys	71	26	3	100
Girls	76	22	2	100
Both sexes	73	24	3	100

Weight and Height Relation.—This relationship has been found by various observers to be a most reliable index of nutrition. As shown in Table 5, these children show a large percentage above the average: 71 per cent. of the boys and 76 per cent. of the girls are in that group, and only 3 per cent. of the boys and 2 per cent. of the girls are 11 per cent. or more below average. It is of interest to note that the five children who are in the last group have been in the institution for less than six months.

Charts 3 and 4 show the distribution of weight for height for the boys and girls, respectively.

Relation of Length of Residence to State of Nutrition.—Twenty children who were in the institution less than 1 year were compared with eighteen children resident 7 years or more. The very marked improvement is shown in Table 6. Although the numbers are small, the difference is so striking that it seems worth noting. Whereas, in the first group the tolerable zone of normality contained 45 per cent. of the children, in the second group it fell to only 17 per cent.

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3. Holt, L. E., and Howland, J.: Diseases of Infancy and Children, Ed. 8, New York, D. Appleton & Co., 1922, p. 23.

TABLE 6.—*State of Nutrition Improved Strikingly by Residence in the Home*

	Above Average	1-10% Below Average	11% or More Below Average
Less than one year: Number	11	8	1
Percentage	55	45	5
Seven years or more: Number	15	3	0
Percentage	83	17	0

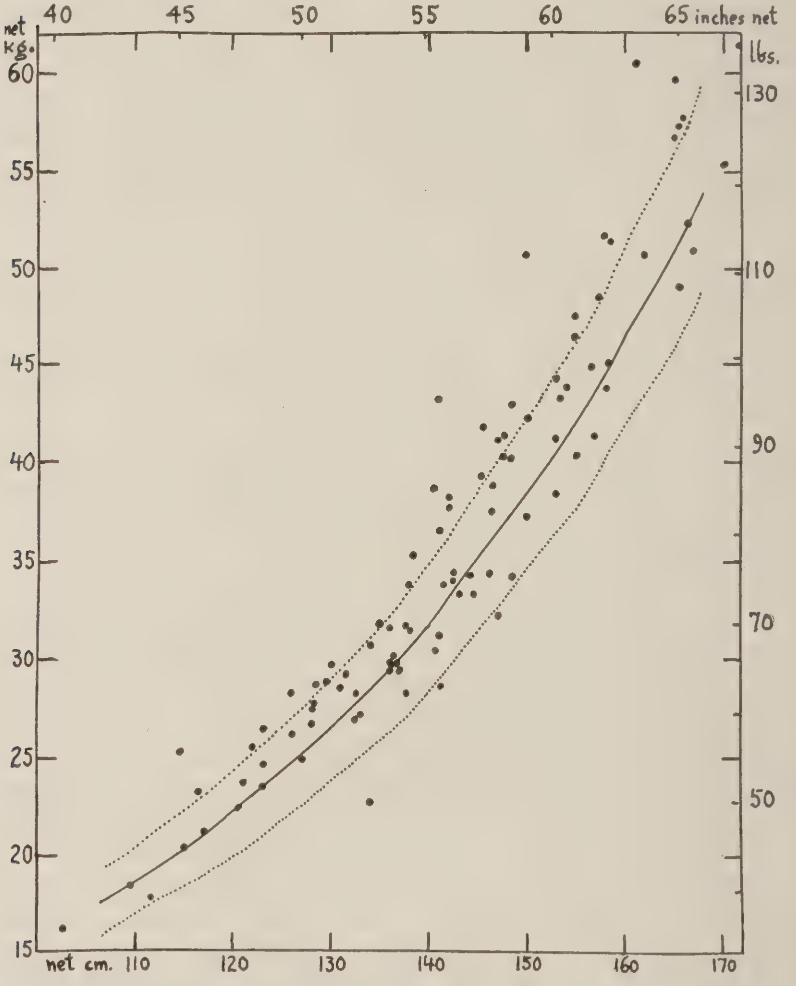

Chart 3.—The distribution of weight for height for ninety-seven boys.

Relation of Parental Tuberculosis to Nutrition of Offspring.—Thirty-five children gave a positive family history for tuberculosis in either one or both parents. The data are represented in Table 7, and are seen to compare badly with Table 5 for all the inmates of the home. Notice the figures in the bottom line of each table.

TABLE 7.—*State of Nutrition Worse in Children of Tuberculous Parents*

	Above Average	1-10% Below Average	11% or More Below Average
Number	13	20	2
Percentage	37	57	6

Relation of Size of Family to Nutrition.—We arbitrarily divided our inmates into two groups: four children or less in one group and five or more into a second group, and compared the state of nutrition of the children in these two groups. The data in Table 8 are negative, i. e., the state of nutrition did not suffer by an increase in the size of the family.

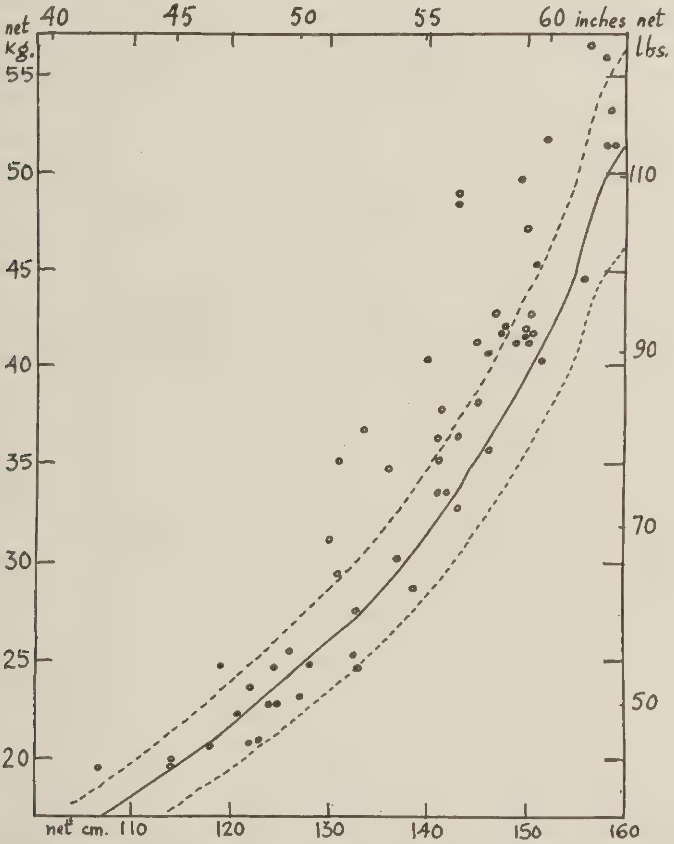

Chart 4.—The distribution of weight for height for fifty-nine girls.

TABLE 8.—*Relation of Size of Family to Nutrition*

	Above Average	1-10% Below Average	11% or More Below Average
Four or less children in family: Number	45	24	5
Percentage	61	32	7
Five or more children in family: Number	38	25	3
Percentage	57	38	5

Relation of Order of Progeny to Nutrition.—There were twenty-seven first-born children. We compared this group with twenty-four children that were either fifth-born or more. The data are given in Table 9. The first-born were more frequently above normal. This finding is contrary to some statements in the literature.

Table 9.—*Relation of Order of Progeny to Nutrition*

	Above Average	1-10% Below Average	11% or More Below Average
First-born: Number	18	7	2
Percentage	67	26	7
Fifth or more born: Number	13	11	0
Percentage	54	46	0

SUMMARY

1. Children of the poorest class, when under proper institutional care, are shown to catch up rapidly to normal children in physical respects. Whether they do so in the intellectual sphere will be dealt with in another paper.

2. The one hundred and fifty-six children studied were generally undersized. Whether that is due to a racial difference or to a retarded development could not be determined.

3. The children studied were in a very good state of nutrition; only 3 per cent. were found to be 11 per cent. or more underweight.

4. The longer they stayed in the institution the larger was the percentage of children who were above the average in nutrition and development.

5. The children found to be in better health were those with no history of parental tuberculosis, and the first-born children. On the other hand, their nutrition did not suffer by an abundance of brothers and sisters.

A MORPHOLOGIC AND QUANTITATIVE STUDY OF THE BLOOD CORPUSCLES IN THE NEW-BORN PERIOD *

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The condition of the blood in the new-born has been studied by numerous investigators since Denis [1] published the first observations on the subject in 1831. In many instances there has been insufficient data to warrant the conclusions submitted. Statistical results, to be of any great value, must be based on a reasonably large group of cases preferably with repeated observations, and this factor apparently has been disregarded in most of the work published on the blood of the new-born.

In practically every case the blood has been studied at twenty-four hour intervals, usually for the first week and occasionally through the first month. Sometimes the first day has been divided into two or three parts in order to follow the changing blood picture of the first twenty-four hours.

A study of the literature on this subject shows that, though very marked changes occur during the first forty-eight hours after birth, little effort has been made to determine the exact times at which the important modifications take place.

At the suggestion of Dr. R. E. Scammon, the present study has been based chiefly on the blood of the new-born during the first forty-eight hours after birth, dividing this interval into nine parts.

The study of the finer structure of the leukocytes during the first few days of life has received less consideration than cell counts and hemoglobin determinations. The fluctuating white blood count during this period promised interesting changes in the morphology of the blood. In this work, therefore, the structural changes in the leukocytes have received primary consideration.

SUMMARY OF LITERATURE

The greater part of the literature, previously published, on the morphology of the blood of the new-born is given here in outline form. There are a few facts, however, that cannot be presented in such an outline and these are briefly discussed below.

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* Received for publication, February 27, 1924.

* From the Department of Anatomy and the Department of Pediatrics, the Medical School, University of Minnesota.

[1] Denis: quoted by Bayer.

TABLE 1.—*Summary of Published Data on the Morphology of the Blood of the New-Born*

Aitkin, J.: J. Obst. & Gynec. Brit. Emp. **1**: 414, 1902
- Hemoglobin.—106 per cent., birth average
- Red Blood Cells (count in millions).—Birth, 6.13; 1st hour, 6.45; 12-24 hours, 7.67; 48 hours, 8.35; 3 days, 7.68; 5 days, 6.75; 7-10 days, 5.89
- Leukocyte Count.—2-16 hours, taken before feeding, 18,525; 2d day, after feeding, 22,800; 3d day, 15,585; relation to meals not noted
- Differential.—Erythroblasts present in all cases directly after birth; present at 48 hours in 24 of 25 smears; present at 5-9 days in 15 of 27 smears; R. B. C. 3¼-10¼ microns in diameter; 14 cases at birth: lymphocytes, 46-66 per cent.; polymorphonuclears, 27-46 per cent.
- Remarks.—Amount of hemoglobin does not vary with number of red blood cells. Increase in leukocyte count after meals average 10,000 per cu. mm.

Takasu, K.: Arch. f. Kinderh. **39**: 346, 1904
- Hemoglobin.—130.2 per cent. first 3 days
- Red Blood Cells (count in millions).—Average first three days, 4.84
- Leukocyte Count.—First 3 days, 13,000 to 28,000; 4-10 days, 14,700 average
- Differential.—Nucleated red blood cells in nearly all cases; eosinophils in the new-born vary from 0 to 9.6 per cent.; average from 2 hours to 10 days, 2.8 per cent.
- Remarks.—Japanese children show racial peculiarity of high hemoglobin

Perlin: Jahrb. f. Kinderh. **58**: 549, 1903
- Hemoglobin.—116-119 per cent. until fourth day
- Red Blood Cells (count in millions).—1st day, 5.71; 2d day, 6.23; 3d day, 6.29; 4th day, 6.14; 5th day, 5.67; begins to drop at 11 days
- Leukocyte Count.—17,146, 1st day; 17,857, 2d day; 16,281, 3d day; 16,960, 4th day; 14,450, 5th day

Karnitzki, A.: Arch. f. Kinder. **36**: 42, 1904
- Hemoglobin.—12.7 gm. per hundred cubic centimeters of blood
- Leukocyte Count.—16,000, 1st day; 16,000, 2d day; 15,300, 3d day
- Differential.—Studied 1,000-1,500 cells in his differentials; polymorphonuclears are larger, thicker and richer in chromatin early in life; neutrophils difficult to distinguish from eosinophils in some smears; believes the eosinophil granules come from the neutrophil nucleus; several degeneration forms noted in infancy
- Remarks.—Hemoglobin does not vary with red cell count

Krüger: Arch. f. path. Anat. **106**: 1, 1866
- Remarks.—Hemoglobin of mother equal to that of new-born; after a few days the hemoglobin of infant is higher

Carstanjen, M.: Jahrb. f. Kinderh. **52**: 215, 333, 1900
- Hemoglobin.—113 per cent., birth average
- Differential.—Polymorphonuclears: 1st day, 73.45 per cent.; 3d day, 66.18 per cent.; 6th day, 41.81 per cent.; 9th day, 36.12 per cent. Lymphocytes: 1st day, 16.05 per cent.; 3d day, 18.84 per cent.; 6th day, 35.11 per cent.; 9th day, 41.86 per cent. Transitionals: 1st day, 8.43 per cent.; 3d day, 11.11 per cent.; 6th day, 17.52 per cent.; 9th day, 18.66 per cent. Mononuclears: 1st day, 0.17 per cent.; 3d day, 0.14 per cent.; 6th day, 0.75 per cent.; 9th day, 0.66 per cent. Eosinophils: 1st day, 1.9 per cent. During first day average nucleated red blood cells equaled 1.3 per 100 leukocytes. First 24 hours polymorphonuclears are highest; polymorphonuclears equal lymphocytes at 6-9 days
- Remarks.—Studied only five cases

Elder, G., and Hutchison, R.: Edinburgh M. J. **41**: 105, 1895
- Hemoglobin.—95-115 per cent., birth average
- Leukocyte Count.—Birth average, 17,884
- Differential.—5-12 erythroblasts per 100 leukocytes at birth; no basophils found
- Remarks.—No more anisocytosis than in adult blood. Studied small number of new-borns

Williamson, C. S.: Arch. Int. Med. **18**: 505 (Oct.) 1916
- Hemoglobin (grams per 100 c.c. blood).—1st day, 23.25; 2d day, 22.78; 3d day, 22.78; 4th to 8th day, 22.12
- Remarks.—Hemoglobin findings agree with those of Leichtenstern

Schiff, E.: Jahrb. f. Kinderh. **34**: 159, 1892

Hemoglobin.—	1st day	2d day	3d day	4th day	5th day
Prague	104.6%	104.2%	100.1%	96.5%	94.0%
Budapest	144.0	135.0	135.0	130.0	132.3

- Remarks.—Quoted by Von Reuss; indicates racial differences in hemoglobin

Fehrsen, A. O. M.: J. Physiol. **30**: 322, 1903
- Hemoglobin.—Birth average, 102-125 per cent.; average fall in first few days, 10 per cent.
- Red Blood Cells (count in millions).—First 24 hours, 4.30 to 7.25
- Leukocyte Count.—Highest value up to 20 hours, 22,500; lowest, 7,600
- Differential.—Erythroblasts always present first 2 hours, never after 13 hours; when the leukocyte count is 18,000+, there is an increase in polymorphonuclears

Table 1.—*Summary of Published Data on the Morphology of the Blood of of the New-Born.—(Continued)*

Heimann, F.: Ztschr. f. Geburtsh. u. Gynäk. **69**: 165, 1911
Hemoglobin.—Reduced in icterus neonatorum; the reduction is proportional to the degree of jaundice. Average mild icterus, 102 per cent.; average moderate icterus, 101 per cent.; average marked icterus, 93 per cent.; average control, 113 per cent.
Red Blood Cells.—Decrease in icterus neonatorum
Leukocyte Count.—No marked difference between normal and icterus neonatorum
Differential.—Erythroblasts more common in icterus neonatorum; no polychromophilia noted; eosinophils are reduced 50 per cent. in icterus neonatorum
Remarks.—Fifty cases of icterus neonatorum were studied and compared with 50 normal new-borns

Lucas, W. P.; Bradford, F. D.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Am. J. Dis. Child. **22**: 525 (Dec.) 1921
Hemoglobin.—1st day, 124 per cent.; 2d day, 122 per cent.; 3d day, 114 per cent.; 4th day, 119 per cent.; 5th day, 112 per cent.
Red Blood Cells (count in millions).—1st day, 5.51; 2d day, 5.35; 3d day, 5.11; 4th day, 5.24; 5th day, 4.98
Platelet Count.—1st day, 305,000; 2d day, 300,000; 3d day, 308,000; 4th day, 310,000; 5th day, 295,000; lowest count, 196,000
Leukocyte Count.—1st day, 19,200; 2d day, 15,300; 3d day, 11,100; 4th day, 10,300; 5th day, 10,900
Differential.—Nucleated red blood cells present in 52 per cent. of cases on first day (1 per 100 leukocytes); 5 per cent. of cases on second day (½ per 100 leukocytes); fine basophilic granules in red blood cells first day, rarely after this

Differential Count:	1st day	2d day	3d day	4th day	5th day
Polymorphonuclears	70	62	58	54	49
Lymphocytes	20	24	27	30	34
Transitionals and Mononuclears	9	11	12	13	15
Eosinophils	1	1	1	1½	3

Remarks.—Hemoglobin in severe icterus neonatorum equal to normal; no reduction in red cell count in icterus

Barbosa, J. M.: Oporto, 1921
Hemoglobin.—1st day average, 160 per cent.; 2d day average, 142 per cent.; 1st 20 days average (males), 146 per cent., (females) 139 per cent.
Red Blood Cells (count in millions).—1st day, 6.34; 2d day, 6.15; 1st 20 days, average (males), 6.56, (females) 5.92
Leukocyte Count.—1st day, 20,581; 2d day, 14,802; 5th day, 13,301; average 20 days, (males) 14,039, (females) 15,104
Differential.—Lymphocytes equal to polymorphonuclears on the fifth day

	Days	Polymorphonuclears	Lymphocytes	Eosinophils
8 cases	1	74	20	1½
4 cases	2	59	24	4
	3	62	23	3½
	4	53	30	3
6 cases	5	47	37	4½

Remarks.—Studied the blood of Portuguese new-borns

Bayer, A.: Diss. Bern. 1881
Red Blood Cells (count in millions).—5 minutes to ¾ hour, 4.41; 3½ hours, 5.43; 1 day, 5.11; 2 days, 4.92; 3 days, 5.12
Leukocyte Count.—¾ hour to 16 days: minimum, 5,700; maximum, 25,000; number of cases not stated
Remarks.—Includes prematures

Slawik, Ernst; Ztschr. f. Kinderh. **25**: 212 (June) 1920
Platelet Count.—Average to 10 days, 320,000; one case, 65,000; highest, 4-6 days
Leukocyte Count.—Polymorphonuclear leukocytosis first few days; lymphocytes appear in excess on fifth or sixth day
Differential.—First day marked anisocytosis of platelets, 1 micron to size of red blood cells; first few days, 50-60 per cent. are medium sized, the remainder mostly larger; after 2 weeks the smaller platelets are in excess; birth average, 6 nucleated red blood cells per 100 leukocytes; present in 14 of 25 cases in second week

Biffi and Galli: Riv. di Clin. Pediat. **1**: 1, 1908
Red Blood Cells (count in millions).—Average 2d day, 7.00
Differential.—In 28 of 29 cases, nucleated red blood cells were present

Gundobin, N.: Jahrb. f. Kinderh. **35**: 187, 1893
Red Blood Cells (count in millions).—6.70 average first few days
Differential.—Leukocytosis at birth due to over ripe elements; on the second day this is less

Woino-Oranski: Quoted by Fehrsen
Red Blood Cells (count in millions).—8.30 average first few days
Leukocyte Count.—Birth average, 16,980; 20 hours, 20,980; 2d day, 25,580

Schiff, Ernst: Jahrb. f. Kinderh. **34**: 159, 1892
Red Blood Cells (count in millions).—1st day, 6.00; 12th day, 6.00

TABLE 1.—*Summary of Published Data on the Morphology of the Blood of of the New-Born.—(Continued)*

Viereck, H.: abstr. Folia. haematol. **1**:36, 1904
Red Blood Cells.—Count in new-born male 4 millions greater than new-born female

Mayers, L. H.: Arch. Int. Med. **30**:478 (Oct. 7) 1922
Red Blood Cells (count in millions).—Birth average, 7.63
Remarks.—No direct relationship between red blood cells and amount of hemoglobin

Drinker, Cecil: Oxford Med. **2**:509, 1920
Differential.—Naked red blood cell nuclei found only in cases of active proliferation of red-forming marrow tissue; same applies to megaloblasts

Cadet: Quoted by Slawik
Red Blood Cells (count in millions).—1st day, 171,000; 8th day, 350,000; gradual rise from 1st to 8th day

Rebaudi: Quoted by Lehndorff
Platelets.—Birth average, 95,000

Morse, M.: Boston M. & Surg. J. **166**:448, 1912
Platelets.—Birth, 100,000 to 412,000; increase in icterus neonatorum
Remarks.—If platelet count at birth is high, it decreases during first week; if low at birth, it increases in first week

Hess and Syderhelm: Abstr. Fol. Haem. Zentral. Organ **18**:112, 1916
Leukocyte Count.—During crying the count increases, often 8,000 per cu. mm.; increase is due to lymphocytes

Fischl, R.: Arch. f. Kinderh. **15**:470, 1892
Differential.—No eosinophils seen until 7th fetal month; eosinophils in the new-born vary from 0.73 to 8.6 per cent.; average 4.13 per cent. nucleated red blood cells

Warfield, L. N.: Am. Med. **12**:457, 1902
Leukocyte Count.—Nucleated red blood cells disappear rapidly first 3 days; the polymorphonuclears are relatively and absolutely increased in number shortly after birth
Differential.—Eosinophils vary from 0.2 to 6.0 per cent., average 1.8 per cent. in new-born; myelocytes and mast cells are rare. The lymphocytes do not equal polymorphonuclears in number until the 11th day

Arneth, J.: Arch. f. Gynaek. **74**:145, 1905
Differential.—A large percentage of the neutrophils are single lobed in the first day; in one case 60 per cent. were single lobed; at 7-8 days, 3, 4 and 5 lobed nuclei are more common, while single lobed nuclei are very uncommon; from the first to the seventh day there is a constant transition from one picture to the other
Remarks.—These findings are checked by Dupérié and Kadisson (quoted by Bayer)

Frank, M.: Ztschr. f. Kinderh. **31**:16 (Nov.) 1921
Differential.—Change from a myeloid to a lymphoid type of blood usually occurs on third or fourth day; though it may occur at thirty-six hours; agrees with Arneth in his result; nothing characteristic in the eosinophil curve; basophils scarce; during the first few days the small lymphocytes are more numerous than the large; in some cases 25 per cent. of the leukocytes were small lymphocytes; azure granules are few and often are entirely absent in new-born blood; in the next few days they become more numerous; the small lymphocytes contain few azure granules whereas the large lymphocytes with pale poorly stained cytoplasm contain many; this is an indication that azure granules in excess denote cell aging

Light, C. A.: New York M. J. **74**:1000, 1901
Leukocyte Count.—The increase in the white count is early and remains present during the entire first two years

Scipiades, E.: Arch. f. Gynaek. **70**:630, 1903
Red Blood Cells.—Drop in red count first day and secondary rise on third day
Leukocyte Count.—Highest on first day count; drops in 2-3 days; secondary rise occurs on seventh day, when the cord separates

Demme: Quoted by Bayer
Leukocyte Count.—First 72 hours breast fed; 1 white blood cell for each 135 red blood cells; artificially fed cases show 1 white blood cell for each 122 red blood cells

1. *The Hemoglobin.*—The work done on the hemoglobin determination in the new-born period shows that the values are higher at this time than at any other period in the child's life. The results of Takasu [2] and

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[2] Takasu, K.: Blutuntersuchungen bei den japanischen Kindern. Arch. f. Kinderh. **39**:346, 1904.

Schiff[3] tend to show that the amount of hemoglobin varies in different races.

2. *The Red Blood Cells.*—Soon after birth there is a rise in the red blood cell count lasting for different time intervals, according to various observers. This rise is followed by a fall in the number, often below the count at birth.

Engelsen[4] was one of the first who noted that there was an increase in the diameter of the red blood cells of the new-born.

Silbermann,[5] one of the pioneers in the study of new-born blood, observed many shadows in the red blood cells due to a lack of hemoglobin. He quotes Ponfeck,[6] who first observed this change. Ponfeck noted that these cells were more numerous in disturbances of the new-born, and that occasionally poikilocytosis could be seen in the new-born's blood.

Hoffmeier[7] is quoted by Silbermann as having first shown that the red blood cells of the new-born did not tend to form in rouleaux.

According to Vierordt,[8] Neumann[9] was one of the first to find nucleated red blood cells in the new-born's blood. Neumann noted that this blood often contained cells which resembled those seen in leukemia.

The majority of those who have studied the new-born blood have found nucleated red blood cells present during the first few days.

Fischl[10] did not find many erythroblasts in new-born blood. On the contrary, he claims that their presence is exceptional. He found them usually in premature children. He further found that the rouleaux formation was normal. Karnitzki,[11] on the other hand, found nucleated red blood cells in the normal nursling seven and one-half months after birth, but no other investigator has noted this in the normal infant.

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[3] Schiff, Ernst: Neure Beiträge zur Haemotologie der Neugeborenen mit besonderer Rüchsicht auf die Abnabelungzeit, Jahrb. f. Kinderh. **34:**159, 1892.

[4] Engelsen, E.: Undersögelser over Blodlegemernes Antal, Hämoglobinmengde og Storrelse. Afhandl. for Doktorgraden: Medicin. Kopenhagen, abstr. Jahresb. ü. d. Leistung. in d. ges. Med. **1:**127, 1884.

[5] Silbermann, O.: Zur Hämatologie der neugeborenen, Jahrb. f. Kinderh. **26:**252, 1887.

[6] Ponfeck: quoted by Silbermann, Footnote 5.

[7] Hoffmeier: quoted by Silbermann, Footnote 5.

[8] Vierordt, H.: Physiologie des Kindersalters, Gerhardt's Handbuch d. Kinderh. **1:**53, 1877.

[9] Neumann: quoted by Vierordt, Footnote 8.

[10] Fischl, R.: Zur Histologie des kindlichen Blutes, Arch. f. Kinderh. **15:** 470, 1892.

[11] Karnitzki, A.: Ueber das Blut gesunder Kinder, Arch. f. Kinderh. **36:** 42, 1904.

Geissler and Japha,[12] Hayem,[13] and Loos[14] conclude that normoblasts do not occur normally in new-born blood, and that their presence must be considered as a pathologic finding.

Schiff[3] experimented on the effect of tying the cord immediately after birth and found that the fall in the red blood count began during the first day. If, on the other hand, the cord was tied after the pulsation ceased, there was a rise in the red count lasting from three to four days, then the drop began and was continuous. In Schiff's work, the counts were all more than 6,000,000 on the first day. Even on the twelfth day after birth, the counts average 6,000,000 cells per cubic millimeter. The red blood counts taken during fasting were greater than after feeding. Viereck,[15] whose study was similar to that of Schiff, obtained quite different results. He found that when the cord was tied late, i. e., after pulsation had ceased, the red count began to descend early. He observed that in twelve cases there was a decrease, and in ten cases an increase in the count after feeding. If the blood was studied immediately after birth, the red blood cell count in the male new-born exceeded that of the female by 400,000.

Cathala and Daunay[16] found a physiologic increase in reticulated red cells at birth, up to 20 per cent. in a few cases. They obtained a decrease in the resistance of the red cells during the first few days after birth. This is in contrast to the observation of De Vicariis[17] who observed an increased resistance of the red blood corpuscles during the first few days.

Several theories have been advanced to explain the increased red blood cell count in the neonatal period. Schiff[3] claims it is due to a concentration of the blood brought about by increased excretion and decreased intake of fluids. Dupérié[18] accounts for the increased cell count by increased bone marrow activity. Hayem holds a similar view. Elder and Hutchison[19] agree with Schiff. They feel that the process must be due to concentration since it is too rapid for hemopoiesis or hemolysis. Hayem believes that the drop in the red blood cell count subsequent to the rise is due to the energetic building of other blood elements. Lépiné[20] accounts for the increased red count by a concentration. The drop is explained by a gain in weight and an increase in plasma. He found that while the weight of the new-born continues to drop the red count stays up. Gundobin[21] explains the change in the red count as being a result of a physiologic need, but the mechanism accounting for the changing counts is not described. Aitken[22] believes that the change in red count is due in part to a peripheral stasis of the blood and favors the concentration theory. Frank,[23] recently, in a paper on new-born blood also upholds the concentration view.

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[12] Geissler and Japha: Beitrag zu den Anämien junger Kinder, Jahrb. f. Kinderh. **53**:627, 1901.

[13] Hayem: quoted by Fehrsen.

[14] Loos, J.: Ueber das Vorkommen kernhaltiger rother Blutzellen bei Kindern, Jahrb. f. Kinderh. **29**:331, 1895.

[15] Viereck, H.: Beiträge zur Hämatologie des Neugeborenen, abstr. Folia. haematol. **1**:36, 1904.

[16] Cathala, V., and Daunay, R.: Les hématies granuleuses, là resistance globulaire a la naissance et pendant les premièrs jours, Compt. rend. Soc. de Biol. **64**:801, 1908.

[17] De Vicariis: Recherches sur le sang des enfants prematures, abstr. Zentralbl. f. norm. Anat. u. Mikrotchn. **3**:174, 1906.

[18] Dupérié: quoted by Bayer.

[19] Elder, G., and Hutchison, R.: Some Observations on the Maternal and Fetal Blood at Birth, Edinburgh M. J. **41**:105, 1895.

3. *The Blood Platelets.*—The literature on the blood platelets in the neonatal period is summarized in Table 1 and requires no special discussion at this point.

4. *The Leukocytes.*—A review of the literature is convincing that the new-born normally has an increased leukocyte count. Many causes have been advanced for this leukocytosis, the following being the more important ones.

(*a*) Blood Concentration: Just as in the case of the red blood cells, the small intake of food during a time in which the output of fluids goes on, causes a concentration of the blood and a rise in the leukocyte count. Schiff favors this view as being responsible, in part at least, for the increased white count.

(*b*) Inflow of Lymph Following Digestion: Schiff believes that in addition to blood concentration the lymph flow carries large numbers of lymphocytes into the circulation.

(*c*) Foreign Protein: As milk in an organism not fed before, Lépiné believes that this digestion has the power of causing the increased count.

(*d*) Peristence of Fetal Leukocytosis: Von Reuss[24] suggests that the condition of leukocytosis is present at birth and is carried over from the intra-uterine period. Scipiades[25] had previously presented this view.

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[20] Lépiné, R.: Blutkörperchen beim Neugeborenen, reviewed, Jahresb. ü. d. Leistung. in d. ges. Med. **1**:165, 1876.

[21] Gundobin, N.: Ueber die Morphologie und Pathologie des Blutes bei Kindern, Jahrb. f. Kinderh. **35**:187, 1893.

[22] Aitken, J.: Blood Counts in the New-Born, J. Obst. & Gynec. Brit. Emp. **1**:414, 1902.

[23] Frank, M.: Beitrag zur Biologie der weiszen Blutzellen in der Neugeburtzheit und im Säuglingsalter, Ztschr. f. Kinderh. **31**:16 (Nov.) 1921.

[24] Von Reuss, A. R.: The Diseases of the New-Born, New York, William Wood & Co., 1921, p. 41.

[25] Scipiades, E.: Beiträge zur Physiologie des Blutes der Neugeborenen in den ersten zehn Lebenstagen, Arch. f. Gynaek. **70**:630, 1903.

(*e*) Traumatic Leukocytosis: Warfield[26] found in his cases that the leukocyte count was higher in difficult labors, so he suggests the possibility of a traumatic leukocytosis.

(*f*) Compensatory Leukocytosis: Arneth[27] believes the condition is due to a compensatory process to take the place of the liver and perhaps of the placenta which are active blood builders before birth. He thinks that the active hemopoiesis does not begin until the third or fourth day of life, when the bone marrow and other blood forming organs are able to take care of the blood formation.

(*g*) Leukocytosis Due to Circulatory Changes: Rieder[28] accounts for the leukocytosis by a sudden change of the circulation with its relations to the various organs.

(*h*) Bone Marrow Activity: Arneth.

(*i*) Pathologic Leukocytosis: According to Gundobin, the leukocytosis is a pathologic state due to a sudden deprivation of food derived through the placenta.

The effect of digestion on the leukocyte count has received much attention. Schiff found that the white count was usually highest after the first feeding. He also found a secondary rise present when the cord became detached. According to Wile,[29] digestive leukocytosis is uncommon in breast fed infants and inconstant in bottle fed infants and in early childhood. Karnitzki found the count to be greater before than after nursing. Warfield found during the first eight hours an average of 26,090 white cells. On the third day there was a decided drop to 13,270. On the eleventh day, due to the taking of more food than on the third day, the count was 16,740. Aitken cautions against the taking of white blood counts without regarding the relationship to food intake. His results are as follows: From two to sixteen hours—always before feeding—average, 18,525; second day, after feeding, 22,800; third day (relation to meals not noted) 15,585.

Aitken observed increases in his counts after feeding, averaging 10,000. Following a long fast, the digestive leukocytosis was found to be more marked. His increase in values varied from 5,000 to 17,000. Gundobin's findings in this regard are of interest. After fasting, he noted a polymorphonuclear leukocytosis. This was not observed until two or three hours after food was taken. The increase was less if there was a pre-existing leukocytosis. It averaged from 2,000 to 3,000. He found that the time of day, temperature of the surroundings, weight of the child and muscular activity did not affect the leukocyte count. Japha [12] disagrees with Gundobin and failed to find a leukocytosis after food as a regular phenomenon. Mitchell [30] found that digestive leukocytosis was inconstant in babies. He observed increased leukocyte counts in the afternoon regardless of the taking of food. He often found a decreased value after feeding, though the count usually rose before the next feeding. When a rise was found after feeding, it occurred very soon after the food ingestion and began to decline in half an hour. Rieder, working on two cases, found an increase in mononuclear leukocytes after food was taken. Groeber [31] in ten cases decided that no conclusions could be made from his work. He found that in six cases, the polymorphonuclears were increased after food intake. In four cases they were decreased. Carstanjen [32] studied fifteen cases. Smears were studied before feeding, and one, two, three, four and five hours after feeding. The white counts are not given. The polymorphonuclears were always higher and the lymphocytes always lower before than after feeding. The average change was about 4 per cent., and was increased after a long fast. Aitken [22] found an increase in the polymorphonuclears of about 7 or 8 per cent. This was not marked on the second and third day.

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[26] Warfield, L. N.: The Differential Leukocyte Count in the New-Born, Am. Med. **12**:457, 1902.

[27] Arneth, J.: Die Leukocytose der Schwangerschaft, während und nach Geburt, und die Leukocytose der Neugeborenen, Arch. f. Gynaek. **74**:145, 1905.

[28] Rieder: quoted by Carstanjen, Footnote 32.

[29] Wile, I. S.: The Leukocytes in Pulmonary Diseases of Children. Arch. Pediat. **26**:195. 1909.

5. *The Differential Leukocyte Count.*—With the rapid changing white blood count of the neonatal period there are equally marked changes in the differential blood picture, as seen in the outline. It is interesting to note the results obtained by Grüneberg [33] in his studies of the blood of the human embryo, which are instructive in showing the development of the blood picture present in the new-born. He found that at 3 months there are a large number of stem cells and only a few large lymphocytes. At this stage the blood closely resembles acute lymphatic leukemia. At from 5 to 6 months the stem cells become less numerous, and transitional leukocytes increase in number. At 7 months the stem cells reappear, and large numbers of polymorphonuclears are found, so that the picture resembles a mixed leukemia. Erythroblasts and megaloblasts are very commonly seen during the first 3 months, but after this period megaloblasts are rarely seen. Atypical cells pass into the circulation during the ninth fetal month.

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30. Mitchell, A. G.: Leukocyte Counts During Digestion in Bottle-Fed Infants, Am. J. Dis. Child. **9**:358 (May) 1915.

31. Groeber: quoted by Carstanjen, Footnote 32.

32. Carstanjen, M.: Wie verhalten sich die prozentigen Verhältnisse der verschiedenen Formen der weissen Blutkörperchen beim Menschen unter normalen Verhältnissen, Jahrb. f. Kinderh. **52**:215-333 1900.

33. Grüneberg, A.: Beitrag zur Morphologie des Blutes menschlichen Embryonen, abstr. Folia Haematol. **6**:185, 1908-1909.

MATERIAL AND METHODS

1. *Time Intervals Employed.*—Seventy-one new-born infants (thirty-one girls and forty boys) were used for the present study.

Examinations were made as soon after birth as possible, and then at approximate six hour intervals up to and including thirty-six hours. The next examination was at forty-eight hours, and a final examination was made at 5 days of age to determine the direction of the curves for the white count, and the various components of the differential.

It was very difficult to study the blood at the exact hourly intervals, so for convenience the following range of hours was used: (1) At birth to one and one half hours after birth, median, one half hour; (2) from five to seven hours after birth, median, six hours; (3) from eleven to thirteen hours after birth, median, twelve hours; (4) from fifteen to twenty-one hours after birth, median, eighteen hours; (5) from twenty-three to twenty-five hours after birth, median, twenty-four hours; (6) from twenty-nine to thirty-one hours after birth, median, thirty hours; (7) from thirty-four to thirty-eight hours after birth, median, thirty-six hours; (8) from forty-six to fifty hours after birth, median, forty-eight hours; (9) five days after birth.

In every case the cord was clamped after pulsation had ceased, the average time being about from two to four minutes.

More than 50 per cent. of the mothers were gravida. In those who had a history of miscarriages, the venereal history of the father, mother and others in the family was thoroughly investigated. Syphilis was absent in all of the cases studied. The mother's urine was examined and in every case was negative except for occasional lactosuria, a trace of albumin or a few leukocytes.

2. *Selection of Material.*—The question of choosing a new-born fitted for study was often difficult. The skin offered an occasional problem. Impetigo of a mild degree was encountered in several cases. Desquamation or generalized dermatitis, lasting for short periods and then disappearing, was not thought sufficient cause for rejection of new-borns.

Temperature elevation cannot be used as a guide for inflammatory conditions because of its frequency in apparently normal new-born children. In many cases, the giving of a few ounces of water caused a drop in the temperature; to be explained on the basis of dehydration. As regards the eye discharges, those cases were included which failed to show bacteria on repeated examinations.

Eclampsia in the mother was in itself not considered sufficient cause for rejection, so long as the infant was entirely normal.

In two instances, tuberculosis was present in the mother. In one case an arrested tuberculous pulmonary infection was present, while the other patient died shortly after childbirth, the cause of death being tuberculous meningitis. The two babies were normal in every respect, the tuberculin reactions were normal, and the gain in weight satisfactory so they were included in the study.

The cases excluded as abnormal were: Those in whom definite infection was proved, any new-born that weighed less than 2,500 gm. was considered premature and not included in the group, and new-born babes with hemorrhagic disease.

Icterus neonatorum was not found to be a cause for excluding the new-born. Almost every baby has some degree of icterus during the first few days. In a few babies with severe icterus the findings were tabulated to compare them with the findings in those who did not show marked icterus.

3. *Hemotologic Technic.*—The blood was obtained in the usual way by pricking the heel. The part was first cleansed with alcohol and ether, and a free flow of blood was always obtained. The first two drops were not used. The blood for study was secured when it flowed without the aid of external pressure.

For the study of the red blood cells Deiner's solution was used. The blood was drawn to 0.5 in the 1 : 100 dilution pipette, and the Deiner's solution was then drawn to 100, making a dilution of 1 : 200. The pipette was shaken for at least five minutes to keep the platelets from clumping. Thus the red cells and platelets were obtained in the one pipette. At first the white cell pipette for 1 : 10 dilution and the red cell pipette for 1 : 100 dilution were both used for the white cell count; with the two different dilutions the counts could be checked. Later, however, this was not done and the 1 : 100 dilution alone was used, for the latter method was found after repeated trials to be the more accurate. The Levy-Zeiss hemocytometer was employed, and in every case repeated drops from the same pipette were used to check results. The pipettes used were standardized, and checked against each other.

Smears of various degrees of thickness were made for differential cell counts and finer cytology. The smears were stained with Wright's modification of the Romanowsky dye. Five hundred cells were included in each differential count.

The complete individual differential counts have been placed on file at the Wistar Institute of Anatomy, Philadelphia.

4. *Classification of Leukocytes and Erythroblasts.*—Throughout the discussion Pappenheim's [34] terminology has been used, the following criteria being used for determining the different types of cells.

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[34] Pappenheim, A.: Clinical Examination of the Blood and Its Technique, New York, William Wood Co., 1914.

(*a*) The Neutrophil, i. e., Polymorphonuclear P. M. N. Leukocyte: The nucleus is lobulated. The cytoplasm is acidophilic, stains pink with Wright's stain, and contains all types of pink granules. Some of these cells contain vacuoles in their cytoplasm.

(*b*) The Lymphocytes: The lymphocytes have been divided into four classes: (1) The small lymphocyte. The nucleus is coarse, and occupies most of the cell. It is surrounded by a narrow rim of greenish blue cytoplasm which may, but usually does not, contain azure granules; (2) the medium lymphocyte. This cell is classified according to size rather than structure. It is about twice the size of a normal red blood cell. The nucleus may form only one half of the cell but often it very nearly fills the cell, much as in the case of the small lymphocyte. The cytoplasm and nuclear structures are as in the small lymphocyte; (3) the large lymphocyte. This term is used to denote the macrolymphocyte of Pappenheim. The nucleus is small, in a cell about the size of the polymorphonuclear. The structure of the nucleus is like that of the small lymphocyte (Fig. 1 *a*); (4) the leukocytoid mesolyphocyte. Much the same as 3 except that the nucleus is smaller and less dense (Fig. 1 *b*).

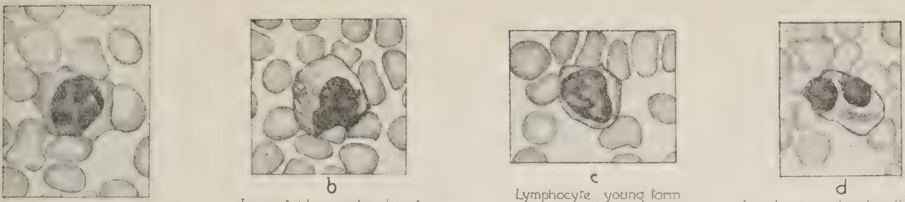
In addition to the above, one often sees younger lymphocytes. These are recognized by the open structure of the nucleus. The chromatin strands are arranged as in a sieve. Usually nucleoli are present in the nucleus (Fig. 1 *c*). One can easily differentiate this nucleus from that of an adult lymphocyte (Fig. 1 *a*) in which the chromatin is arranged in coarse clumps. In the case of the Türke cell, the nucleus is of the early type, and is situated eccentrically.

Lymphocytes having undergone division often appear in the blood stream. The cell is usually large and contains two similar nuclei (Fig. 1 *d*).

(*c*) The Large Mononuclear Leukocyte: The cell is about the size of a large lymphocyte. The cytoplasm is usually a pale blue-green. The nucleus occupies a great part of the cell and has a moderately open chromatin network as compared with Figures 1 *a* and 1 *c*.

(*d*) The Transitional Leukocyte: The cell contains a horseshoe shaped nucleus in a green-blue cytoplasm. It is about the size of a large mononuclear leukocyte. The granules present in cells with basophilic cytoplasm described above are azure. They may be fine, medium, or coarse and are present in varied arrangements. Usually they are more numerous in the larger cells of this group.

(*e*) The Eosinophilic Polymorphonuclear Leukocyte: The nucleus is similar to that of the P. M. N. neutrophil. The cytoplasm is usually filled with coarse red granules.

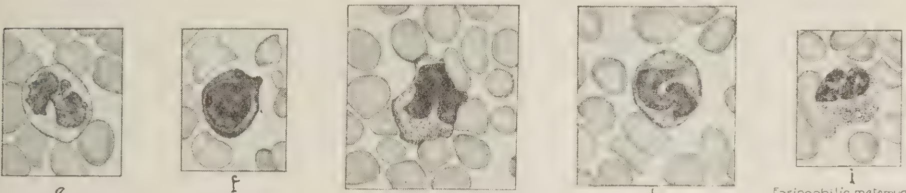


a
Large lymphocyte

b
Leucoytoid mesolymphocyte

c
Lymphocyte . young form

d
Lymphocyte-nucleus has divided



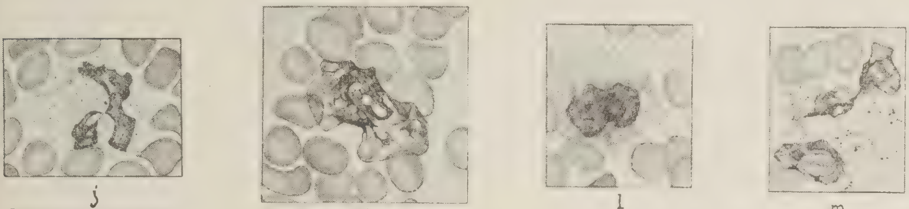
e
Rieder cell

f
Plasma cell

g
Unclassified cell

h
Neutrophilic metamyelocyte

i
Eosinophilic metamyelocyte

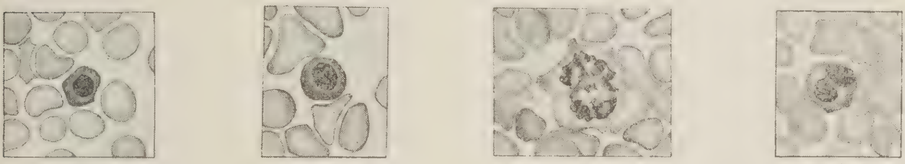


j
Degenerating neutrophile

k
Degenerating lymphocyte -basket form

l
Degenerating lymphocyte

m
Degenerating eosinophile

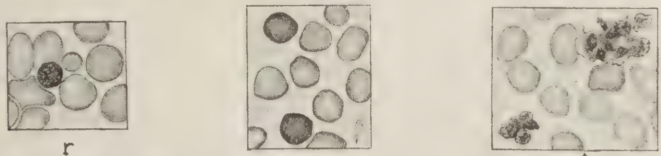


n
ucleated red blood cell - Type II

o
Nucleated red blood cell -Type IV

p
Megaloblast in mitosis

q
Nucleus in normoblast.
dividing



r
Naked normoblast nucleus

s
Polychromatophilia in red cells
Note poikilocyte

t
Group of platelets

Fig. 1.—(*a*) Large lymphocyte, (*b*) leukocytoid mesolymphocyte, (*c*) lymphocyte—young form, (*d*) lymphocyte—nucleus has divided, (*e*) Rieder cell, (*f*) plasma cell, (*g*) unclassified cell, (*h*) neutrophilic metamyelocyte, (*i*) eosinophilic metamyelocyte, (*j*) degenerating neutrophil, (*k*) degenerating lymphocyte—basket form, (*l*) degenerating lymphocyte, (*m*) degenerating eosinophil, (*n*) nucleated red blood cell, Type II, (*o*) nucleated red blood cell, Type IV, (*p*) megaloblast in mitosis, (*q*) nucleus in normoblast dividing, (*r*) naked normoblast nucleus, (*s*) polychromatophilia in red cells (note poikilocyte), (*t*) group of platelets.

(*f*) The Basophilic Polymorphonuclear Leukocyte: The nucleus is usually irregular and pale. The granules stain a purplish blue.

(*g*) The Rieder Cell: The cytoplasm is basophilic. The nucleus is irregular, usually indented on both sides. It is distinctly an irritation type of cell (Fig. 1 *e*). The same nucleus may be present in a cell with neutrophilic cytoplasm, in which case the cell is a Rieder cell in the myeloid series.

(*h*) The Plasma Cell: The cytoplasm is a very deep blue and contains no granules. The nucleus has a cart wheel structure and is usually eccentrically placed (Fig. 1 *f*).

(*j*) The Unclassified Cell: So called because it could not be included in the classification of Pappenheim. It is apparently an irritation type. The cell is about the size of a large mononuclear leukocyte. The nucleus is usually single but it is twisted on itself in an irregular manner, or may be broken up into two unequal parts. The cytoplasm is a muddy, bluish red, and contains both coarse and medium azure granules as well as dust-like neutrophilic granules, like those seen in the neutrophilic promyelocyte. Probably the cell represents a promyelocyte stage in which the nucleus is developing at a greater rate than the cytoplasm (Fig. 1 *g*).

(*j*) The Neutrophilic Myelocyte: Its size is that of a P. M. N. neutrophil. The structure of the two cells is similar except that the nucleus in the myelocyte is not lobed and is less dense.

(*k*) The Eosinophilic Myelocyte: The same as eosiniphilic P. M. N. except that the nucleus is not lobed.

(*l*) The Neutrophilic Metamyelocyte: This includes all neutrophilic cells in which the nucleus is not spherical, but is still undivided. All shapes of nuclei are observed; the one most commonly seen is shown in Figure 1 *h*. Many of these cells are in reality irritation types of P. M. N. neutrophils, but are classed as metamyelocytes because the nucleus is not lobed.

(*m*) The Eosinophilic Metamyelocyte: An eosinophil with a horseshoe shaped nucleus (Fig. 1 *i*).

(*n*) Degeneration Forms: (1) The neutrophilic leukocytes are of several types. The most common one has a dark, fairly easily recognizable nucleus surrounded by groups of neutrophil granules in an irregular mass of cytoplasm. Often a large fan-like mass of light staining substance projects from the end of one of the nuclear fragments (Fig. 1 *j*); (2) the lymphocytes, the form most commonly met, is the large basket-like form with no definite structure present. At times, one sees the beginning formation of the basket effect from one corner of the nucleus of an otherwise fairly intact lymphocyte. One occasionally sees a fairly normal lymphocyte nucleus surrounded by small masses of greenish cytoplasm. Still another type is the ragged, irregular lymphocyte nucleus without any surrounding cytoplasm (Fig. 1 *k* and l); (3) in the eosinophilic leukocytes, one sees a fairly intact nucleus surrounded by irregularly scattered, large, eosinophil granules. The granules often stain darker than normal eosinophil granules. Here too, the nucleus may be breaking up into a basket form (Fig. 1 *m*).

(*o*) The Nucleated Red Blood Cells: For convenience these are divided into four groups: (1) The cytoplasm is red, i. e., contains hemoglobin. The nucleus is condensed. (2) The cytoplasm is polychromatophilic. The nucleus is condensed (Fig. 1 *n*). (3) The cytoplasm is red. The nucleus has an open structure. (4) The cytoplasm is polychromatophilic. The nucleus is similar to that in 3 (Fig. 1 *o*). The term megaloblasts is used for enlarged, nucleated red blood cells. These may be classed 1, 2, 3 or 4.

In addition, one sees an occasional mitotic figure in the nucleated red blood cells (Fig. 1 *p*).

5. *Numerical and Graphical Treatment of Data.*—Since a considerable portion of this work deals with the numerical consideration of the absolute and relative number of the various types of cells in the blood stream, it is important that these figures are examined with some of the simpler analytic and graphic methods which are now applied to biologic problems of this nature. The following program of analysis was therefore carried out in connection with this material.

(*a*) The observations for each of the various types of cells studied were grouped in their time intervals, as outlined in the preceding section, and the central tendency and the dispersion of the data determined. The central tendency was calculated by two methods; first, by the usual arithmetic mean or average; and second, by the median. The determination of the average needs no description but the median is less familiar. The median is the middle value in a series of observations. It is determined by arranging the observations in order of magnitude from the smallest to the largest, and establishing the middle observation by counting from either end of the series. In a large series of observations, if the distribution of cases is symmetrical, the median will approach closely the average. In most series of observations, the number of cases and the character of the distribution does not produce a median exactly equivalent to the average, but the measure is often of value because it does not overemphasize the extreme cases in the group. The dispersion of the data from the average was determined by computing the standard deviation and the coefficient of variability. The standard deviation, which is now recognized as a routine method of determining the absolute variability of a value, is the square root of the average of the squares of the departure of each observation from the average of the entire series of observations. It is commonly expressed by the formula:

$$SD = \sqrt{\frac{d^2}{N}}$$

where SD is the standard deviation, d^2 is the sum of the squares of the deviations of the individual observations from the average and N is the number of the cases in the series. The standard deviation is an absolute number, such as grams if the original observations are in grams, or centimeters if they are in centimeters. To reduce this to a relative number, in the form of a percentage of the average, so that the variabilities of unlike values may be compared, the standard deviation is converted into the coefficient of variability by the formula:

$$CV = \frac{SD}{A} \times 100$$

where CV is the coefficient of variability, SD is the standard deviation and A is the average of the series of observations. In other words, the coefficient of variability is the standard deviation divided by the arithmetic mean or average and multiplied by 100 to put the result in the form of a per cent. of the average.

(*b*) The data and results of this series of computations were placed in graphic form by plotting two series of charts. The first series are field charts having one sort of abcissae (time in hours) and two sets of ordinates (absolute and percentage number of cells). The individual counts were plotted on the fields thus established; the solid dots being used to indicate the relative cell count, and the open circles the absolute cell count.

In the second series of charts the abcissae and ordinates were drawn as in the preceding, and the absolute averages and the percentage averages were indicated by point to point curves, solid lines being used for the former and broken lines for the latter.

(*c*) The results expressed graphically in the series of charts were arranged in tabular form and constitute Tables 2 to 18 of the present study. These tables include the following data: (1) the range and the median of the time intervals used in the study, (2) the number of cases for each interval, (3) the central tendency of both the absolute and percentage values for each interval, (4) the variability as indicated by the maximum and minimum values in each given set of observations as, and (5) the degree of variability as indicated by the standard deviation and the coefficient of variability.

OBSERVATIONS

1. *The Red Blood Cell Count.*—The values of the red blood cell counts obtained are shown in Figures 2 and 3 and in Table 2. The curve of the red count at the different time intervals (Fig. 3), shows a marked rise during the first six hours, from 5.2 to 5.65 million. This is temporary, for, at twelve hours a definite drop has occurred. This decline continues until eighteen hours after birth, after which time the count remains about the same as that of the eighteen hour period, 5.4

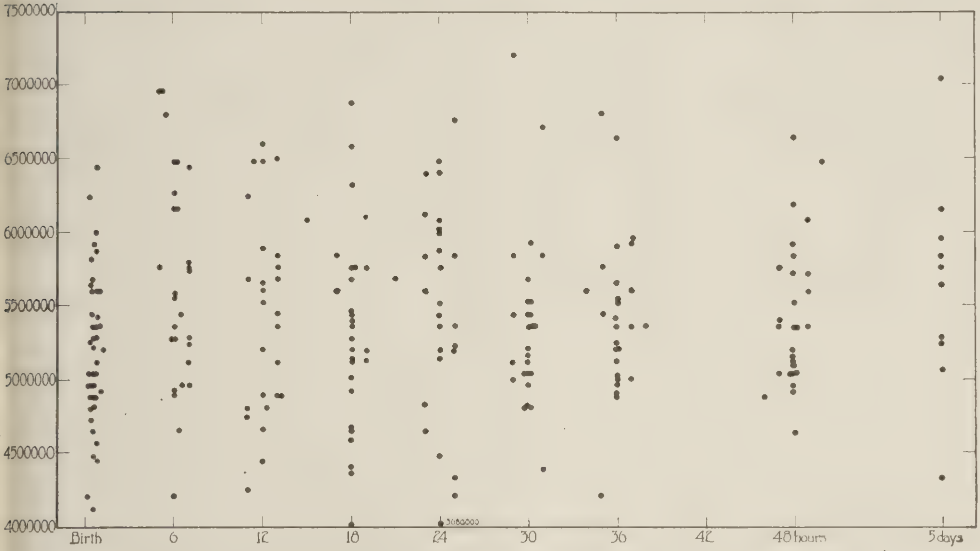


Fig. 2.—The distribution of the absolute counts of red blood cells.

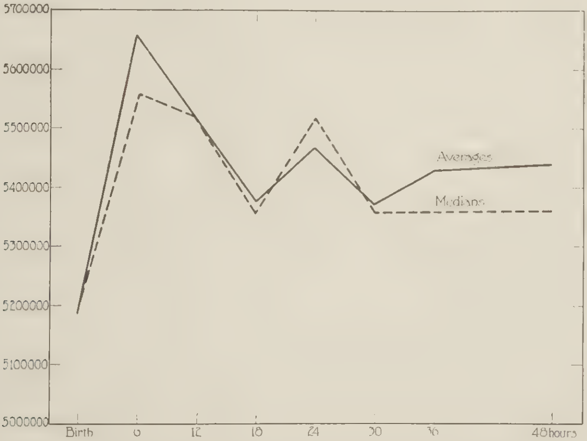


Fig. 3.—The absolute counts of red blood cells.

million. The early ascent is interesting and corresponds to the rise obtained by other investigators. It is unlike the rise taken by the leukocytes which continues until twelve hours after birth. These counts are not nearly so high as those of many other observers, and in most cases the maximum figures correspond fairly closely with other observer's averages. The median curve follows the average curve.

TABLE 2.—*Red Blood Corpuscles Per Cubic Millimeter*

Age (Hours)		Average (Million)	Median (Million)	Maximum (Million)	Minimum (Million)	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
Median	Range							
0.5	0 to 1.5	5.19	5.22	6.44	4.12	51.62	9.93	41
6	5 to 7	5.66	5.56	6.96	4.20	70.39	12.44	28
12	11 to 13	5.52	5.52	7.60	4.24	68.95	12.49	27
18	15 to 21	5.38	5.36	6.88	4.00	65.06	12.09	30
24	23 to 25	5.47	5.52	6.76	3.68	74.25	13.57	27
30	29 to 31	5.37	5.36	7.20	4.38	57.23	10.66	27
36	34 to 38	5.43	5.36	6.80	4.20	52.07	9.59	27
48	46 to 50	5.44	5.36	6.64	4.64	49.15	9.03	28

2. *The Platelet Count.*—Variations of from 10 to 20,000 platelets per cubic millimeter can be considered within the limits of mechanical error because of the difficulty in making this type of count. At birth, as can be seen in Figures 4 and 5 and Table 3, the count is highest, the average being 213,000. During the first six hours there is a sudden drop in the number of platelets, followed by a slower decrease until eighteen hours after birth, and then by a tendency to increase slowly.

TABLE 3.—*Platelets Per Cubic Millimeter*

Age (Hours)		Average	Median	Maximum	Minimum	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
Median	Range							
0.5	0 to 1.5	213,000	196,000	500,000	112,000	91.1	42.8	41
6	5 to 7	179,000	160.000	346,000	108,000	65.2	36.4	28
12	11 to 13	181,000	156,000	460,000	101,000	83.4	46.1	27
18	15 to 21	172,000	165,000	324,000	100,000	52.5	30.3	30
24	23 to 25	191,000	164,000	372,000	103,000	77.1	40.4	27
30	29 to 31	186,000	176,000	330,000	90,000	59.4	31.9	27
36	34 to 38	180,000	165.000	290,000	82,000	51.3	28.5	27
48	46 to 50	192,000	180,000	348,000	95,000	55.2	28.8	28

In the few cases of icterus neonatorum of marked degree, neither the decrease in platelet count observed by Heimann[35] nor the increase described by Morse[36] was found. The averages tend to be the same as in the normal. Nothing unusual in this regard was noted the first two days before the icterus became marked.

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35. Heimann, F.: Zur Lehre des Icterus Neonatorum, Ztschr. f. Geburtsh. u. Gynäk. **69**:165, 1911.

36. Morse, M.: The Blood Platelets in Normal Women, in Obstetrical Patients, and in the New-Born, Boston M. & Surg. J. **166**:448, 1912.

3. *The Total Leukocyte Count.*—By far the most interesting phase in the study of new-born blood is that of the white cell count and differential. Figures 6 and 7 and Table 4 show the leukocyte counts at the different time intervals.

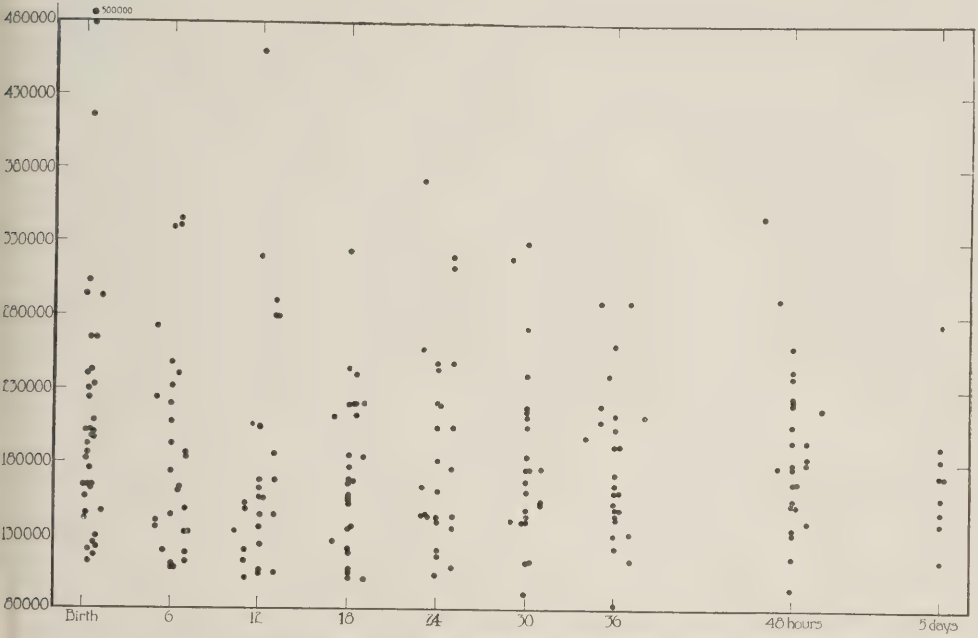

Fig. 4.—The distribution of the counts of absolute number of platelets.

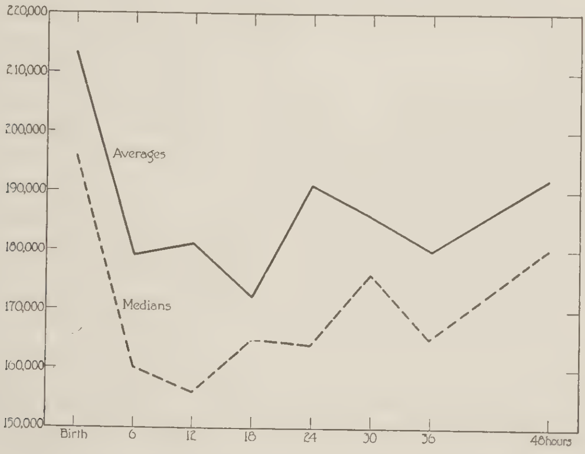

Fig. 5.—The absolute counts of platelets.

At birth, the count is almost always higher than in the normal adult, the average being 16,000. The count rises rapidly until six hours after birth, it then rises at a slower rate, until twelve hours after birth, when it is 22,500. After this period there is a definite descent at about the same rate as that of the ascent. Between twenty-four and thirty hours the count is almost stationary but thereafter there is a gradual fall until five days after birth.

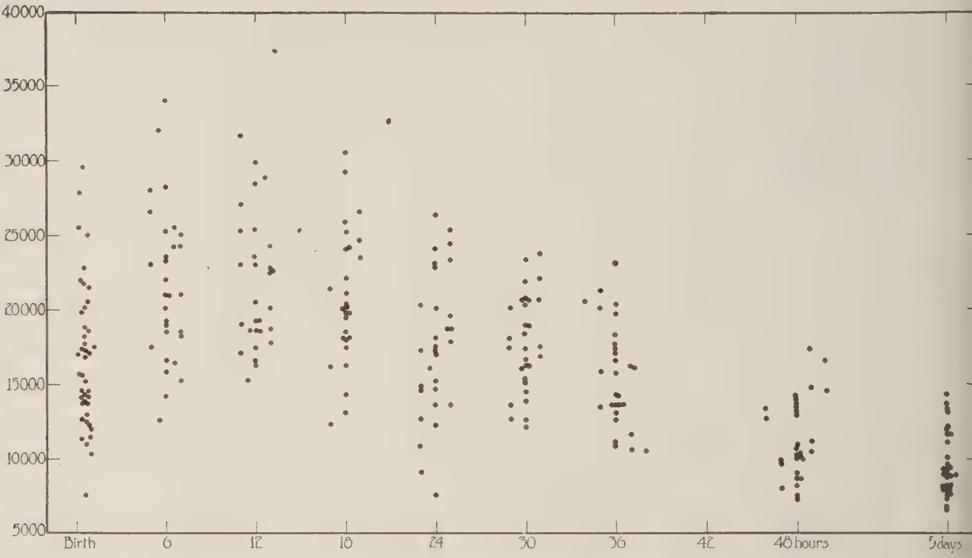

Fig. 6.—The distribution of absolute counts of white blood corpuscles.

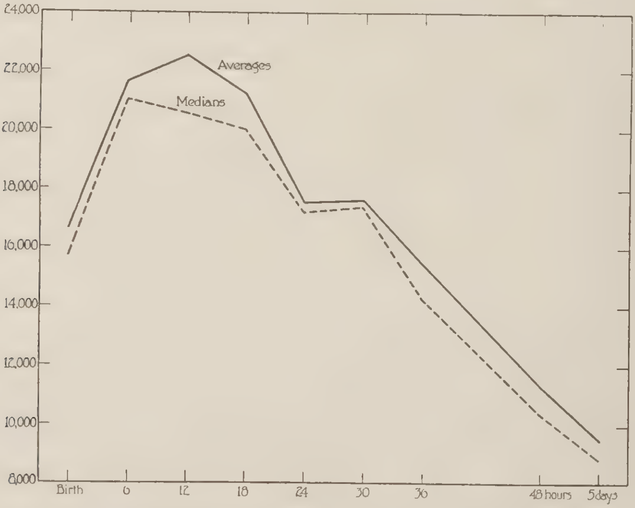

Fig. 7.—The absolute counts of white blood corpuscles.

TABLE 4.—*White Blood Corpuscles Per Cubic Millimeter*

Age (Hours) Median	Age (Hours) Range	Average	Median	Maximum	Minimum	Standard Deviation (Thousands)	Coefficient of Variability	Number of Cases
0.5	0 to 1.5	16,600	15,700	29,600	7,600	5.18	31.2	42
6	5 to 7	21,000	21,000	34,000	12,600	5.08	23.5	30
12	11 to 13	22,500	20,500	37,500	15,200	5.26	23.4	30
18	15 to 21	21,200	20,000	30,400	12,200	4.52	21.3	30
24	23 to 25	17,500	17,200	26,200	7,500	4.70	26.9	30
30	29 to 31	17,600	17,400	23,600	12,000	4.20	23.9	30
36	34 to 38	15,400	14,200	23,000	10,400	3.46	22.5	30
48	46 to 50	11,300	10,300	17,200	7,200	2.61	23.1	30
5 days		9,500	8,800	14,200	6,500	2.52	26.5	30

4. *The Differential Leukocyte Count.*—The average differential leukocyte count follows a definite course during the first few days of postnatal life, but the individual counts show a high degree of variability.

Occasionally there is little difference in the differential study from one period to another in the first eighteen hours, usually there is a rapid change in the blood picture.

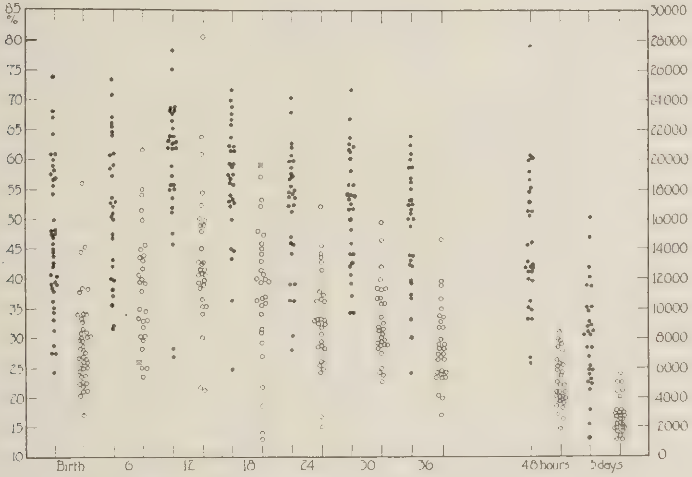

Fig. 8.—The distribution of absolute and percentage counts of polymorphonuclear neutrophil leukocytes. Solid dots, percentage counts; circles, absolute counts.

(*a*) The Polymorphonuclear Neutrophilic (P. M. N.) Leukocytes: A study of the P. M. N. neutrophils is very interesting, since these cells apparently determine the fluctuating white cell count. Figures 8 and 9 and Table 5 indicate that when the percentage values of the P. M. N.'s are averaged, a curve is obtained which shows an ascent until twelve hours after birth, followed by a slow descent. However, when the absolute values are studied, one finds a curve almost identical with that of the total white count.

(*b*) The Neutrophilic Metamyelocytes: As has been previously mentioned, these cells differ from the P. M. N. neutrophil in that their nucleus is single but not spherical. Figures 10 and 11 and Tables 6 show that the incidence of these cells follows very closely that of the P. M. N. neutrophils, with the exception that the apex of the curve occurs at six hours and a slight secondary rise occurs at eighteen hours after birth. After this, there is a gradual descent of the curve.

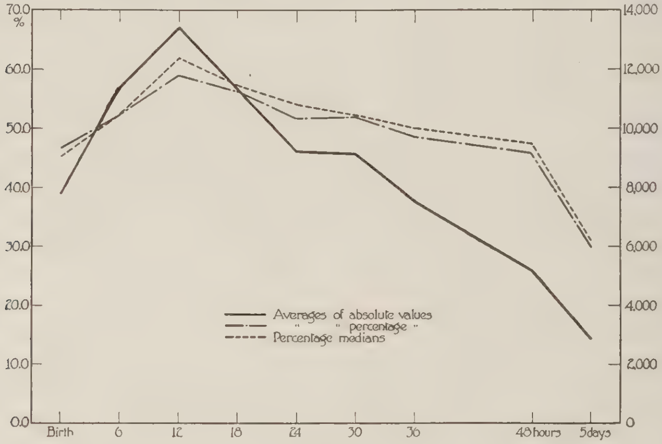

Fig. 9.—Absolute and percentage counts of polymorphonuclear neutrophil leukocytes.

Table 5.—*Absolute and Percentage Number of Polymorphonuclear Neutrophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	46.7 **7,798**	45.4 **7,257**	74.0 **18,500**	27.2 **2,823**	12.040 **2,975**	25.8 **38.15**	40
6	5 to 7	52.3 **11,425**	52.2 **11,900**	73.4 **20,740**	32.0 **5,411**	11.557 **3,850**	22.1 **33.70**	30
12	11 to 13	59.1 **13,491**	62.0 **12,728**	78.2 **28,200**	26.8 **4,422**	11.229 **4,890**	19.0 **36.25**	30
18	15 to 21	56.4 **11,264**	57.4 **11,886**	71.8 **19,797**	24.6 **1,272**	9.569 **4,508**	17.0 **40.02**	30
24	23 to 25	51.6 **9,207**	54.0 **9,106**	70.4 **16,896**	28.6 **2,145**	10.311 **3,255**	20.0 **35.35**	30
30	29 to 31	51.9 **9,177**	52.4 **8,694**	71.6 **15,812**	34.4 **5,136**	9.630 **2,547**	18.6 **27.75**	30
36	34 to 38	48.6 **7,540**	50.0 **7,504**	63.8 **14,674**	24.4 **2,806**	9.982 **2,548**	20.5 **33.79**	30
48	46 to 50	45.9 **5,161**	42.4 **4,809**	74.0 **8,429**	25.8 **1,929**	3.319 **1,714**	7.2 **33.21**	30
5 days		30.0 **2,895**	30.8 **2,898**	50.4 **5,491**	13.0 **1,185**	8.413 **1,171**	28.0 **40.44**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

Here, as in other curves, one can see the value of obtaining the absolute cell counts, which are considerably different from those of the percentage values.

In one case (45), 8.5 per cent. of the leukocytes were metamyelocytes at birth, whereas at eighteen hours, with approximately the same total number of leukocytes, there was 43.0 per cent. metamyelocytes, the highest percentage of this cell observed in the present study.

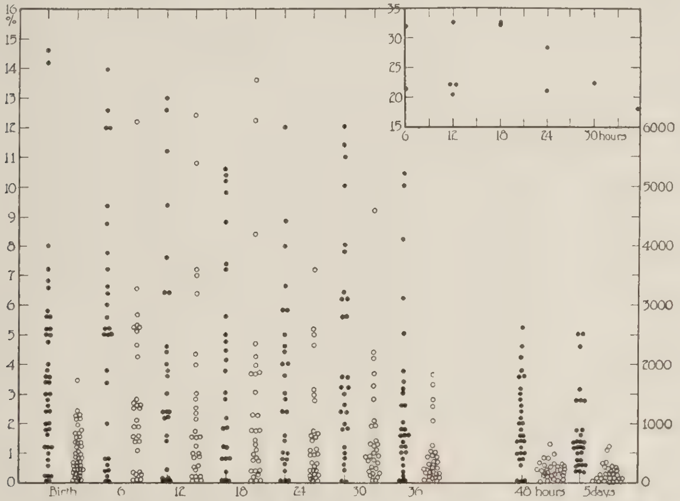

Fig. 10.—The distribution of absolute and relative counts of neutrophil metamyelocytes. Solid dot, percentage counts; circles, absolute counts.

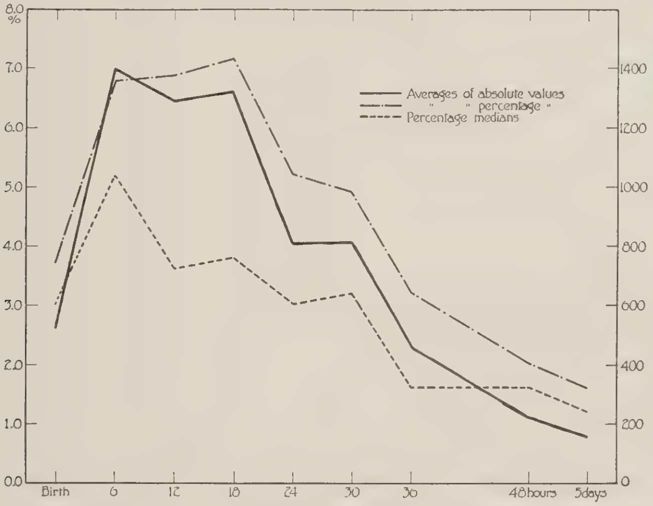

Fig. 11.—Absolute and percentage counts of neutrophil metamyelocytes.

(*c*) The Neutrophilic Myelocytes: These are not so commonly met as one would expect from the large numbers of metamyelocytes. During the first twelve and eighteen hours they are occasionally seen, but

Table 6.—*Absolute and Percentage Number of Neutrophil Metamyelocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.7 **520**	3.0 **432**	14.6 **1,732**	0.0 **0.0**	3.178 **620.26**	85.89 **119.28**	42
6	5 to 7	6.8 **1,399**	5.2 **1,260**	32.0 **6,080**	0.0 **0.0**	6.735 **1294.81**	99.04 **92.55**	30
12	11 to 13	6.9 **1,293**	3.6 **756**	32.6 **6,160**	0.0 **0.0**	7.53 **1553.92**	108.74 **117.10**	30
18	15 to 21	7.2 **1,327**	3.8 **876**	43.0 **6,804**	0.0 **0.0**	10.344 **1647.78**	143.66 **124.17**	30
24	23 to 25	5.2 **804**	3.0 **496**	28.2 **3,570**	0.0 **0.0**	6.398 **851.76**	123.03 **106.47**	30
30	29 to 31	4.9 **814**	3.2 **450**	22.4 **4,592**	0.0 **0.0**	4.751 **925.25**	96.96 **113.67**	30
36	34 to 38	3.2 **459**	1.6 **314**	18.0 **2,340**	0.0 **0.0**	3.870 **540.38**	120.93 **117.73**	30
48	46 to 50	2.0 **213**	1.6 **202**	5.2 **650**	0.0 **0.0**	1.319 **131.26**	65.95 **61.62**	30
5 days		1.6 **155**	1.2 **95**	5.0 **607**	0.0 **0.0**	1.322 **139.14**	82.62 **89.77**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

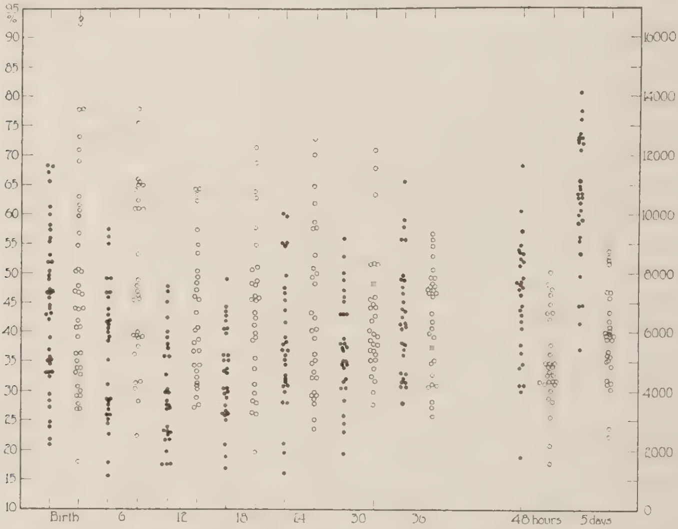

Fig. 12.—The distribution of absolute and percentage counts of combined lymphocytes. Solid dots, percentage counts; circles, absolute counts.

after this time they are rare. A curve of their incidence was not made, because of their infrequent occurrence.

(*d*) The Lymphocytes: The percentage of lymphocytes is fairly high (44.7 per cent.) at birth. The values first descend until twelve hours after birth, and then ascend gradually. They are at the peak of the curve after five days. Figures 12 and 13 and Table 7 show how easily one may be misled by relying on percentage values. When this curve is compared with the curve of P. M. N. percentages one sees that the two are almost the reverse of each other. At forty-eight hours they equal each other, after which time the percentage of lymphocytes is greater than that of the neutrophils (Fig. 14).

On the other hand, on plotting the absolute values of the lymphocytes, one sees an entirely different result. The highest values are present during the first six hours, and after this there is a gradual decrease in the absolute number until forty-eight hours. A slight secondary rise occurs between forty-eight hours and five days.

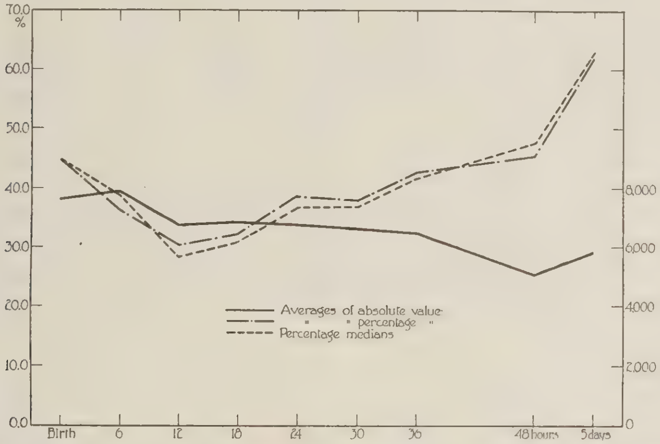

Fig. 13.—Absolute and percentage counts of combined lymphocytes.

Table 7.—*Absolute and Percentage Number of Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	44.7 **7,618**	44.6 **6,832**	67.2 **16,680**	21.2 **1,647**	13.481 **3,545**	30.16 **46.54**	42
6	5 to 7	36.4 **7,890**	38.8 **7,445**	57.0 **13,648**	15.6 **2,556**	11.157 **2,907**	30.65 **36.85**	30
12	11 to 13	30.1 **6,704**	28.4 **6,256**	47.2 **10,986**	17.6 **3,560**	10.381 **2,286**	34.49 **34.10**	30
18	15 to 21	32.1 **6,848**	30.8 **7,120**	49.4 **12,342**	9.8 **2,058**	8.761 **2,558**	27.29 **37.36**	30
24	23 to 25	38.7 **6,766**	37.0 **6,271**	60.2 **12,650**	16.4 **2,898**	10.939 **2,741**	28.27 **40.51**	30
30	29 to 31	38.0 **6,672**	37.0 **6,160**	56.2 **12,251**	19.6 **3,600**	8.788 **2,054**	23.13 **30.78**	30
36	34 to 38	42.9 **6,540**	41.8 **7,314**	65.6 **9,402**	28.2 **3,297**	9.119 **1,759**	21.26 **26.89**	30
48	46 to 50	45.8 **5,110**	48.0 **4,989**	68.0 **8,187**	19.2 **1,632**	10.240 **1,527**	22.36 **29.89**	30
5 days		62.4 **5,924**	63.2 **5,985**	80.8 **8,860**	37.4 **2,505**	11.118 **1,540**	17.82 **26.00**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

When the various types of lymphocytes are graphed one obtains curves which are very similar. In the case of the small lymphocytes (Figs. 15 and 16 and Table 8) there is a secondary rise at twenty-four hours followed by a gradual fall. The small lymphocytes are, as a rule, fully twice as numerous as the large lymphocytes. The leukocytoid mesolymphocytes are not so commonly seen as are the large lymphocytes.

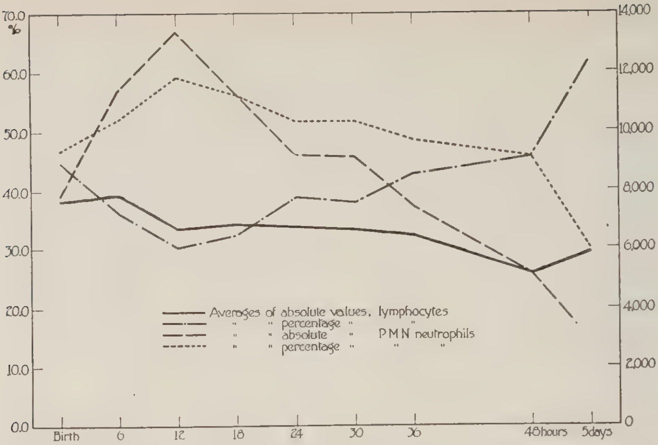

Fig. 14.—The relationship between the absolute and percentage counts of the polymorphonuclear neutrophil leukocytes and the lymphocytes. Solid line, average of absolute counts of lymphocytes; dot and dash line, average of percentage counts of lymphocytes; broken line, average of absolute counts of polymorphonuclears; dotted line, average of percentage counts of polymorphonuclears.

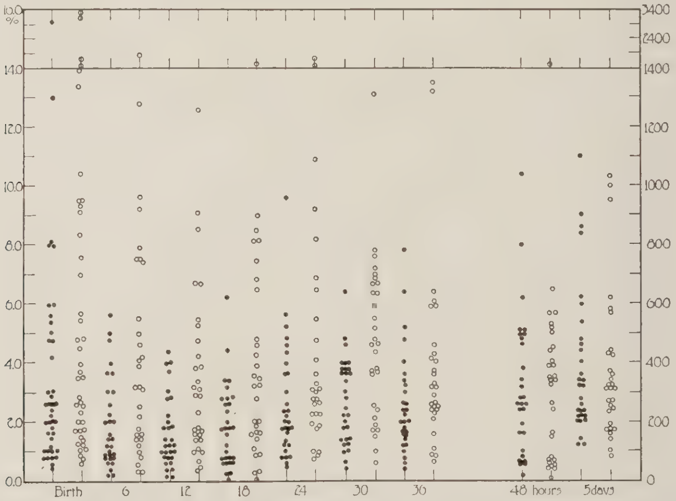

Fig. 15.—The distribution of absolute and percentage counts of small lymphocytes. Solid dots, percentage counts; circles, absolute counts.

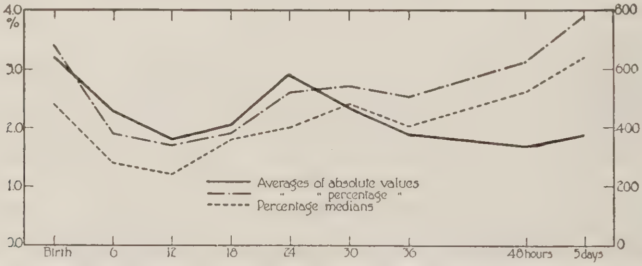

Fig. 16.—Absolute and percentage counts of small lymphocytes.

Table 8.—*Absolute and Percentage Number of Small Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.4 **636**	2.4 **268**	15.6 **3,315**	0.4 **61**	3.228 **714.61**	94.94 **112.18**	42
6	5 to 7	1.9 **451**	1.4 **322**	5.6 **1,879**	0.2 **35**	1.479 **401.56**	77.84 **89.04**	30
12	11 to 13	1.7 **352**	1.2 **291**	4.4 **1,267**	0.2 **37**	1.174 **285.36**	69.06 **81.07**	30
18	15 to 21	1.9 **403**	1.8 **320**	6.2 **1,556**	0.0 **36**	1.378 **340.61**	72.53 **84.52**	30
24	23 to 25	2.6 **581**	2.0 **319**	9.6 **4,231**	0.4 **80**	1.939 **786.20**	74.58 **135.32**	30
30	29 to 31	2.7 **474**	2.4 **475**	6.4 **1,312**	0.4 **69**	1.424 **263.39**	52.74 **55.57**	30
36	34 to 38	2.5 **379**	2.0 **324**	7.8 **1,356**	0.0 **78**	1.714 **303.94**	68.56 **80.20**	30
48	46 to 50	3.1 **335**	2.6 **345**	10.4 **1,518**	0.2 **17**	2.295 **290.20**	74.03 **86.63**	30
5 days		3.9 **375**	3.2 **312**	11.0 **1,035**	1.2 **86**	2.491 **247.44**	62.27 **65.98**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

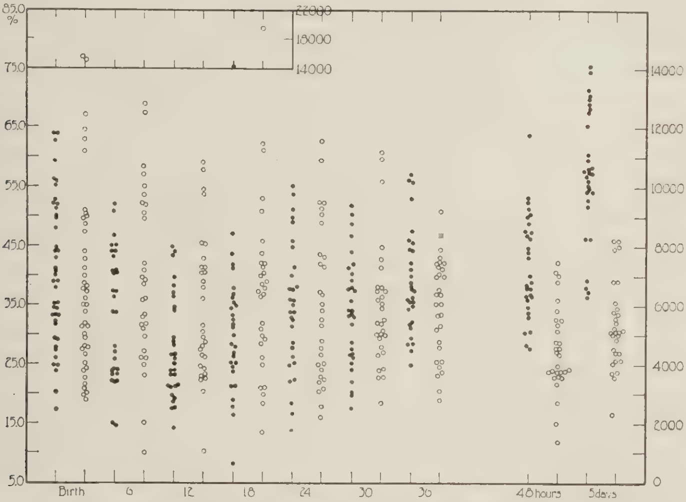

Fig. 17.—The distribution of absolute and percentage counts of medium lymphocytes. Solid dots, percentage counts; circles, absolute counts.

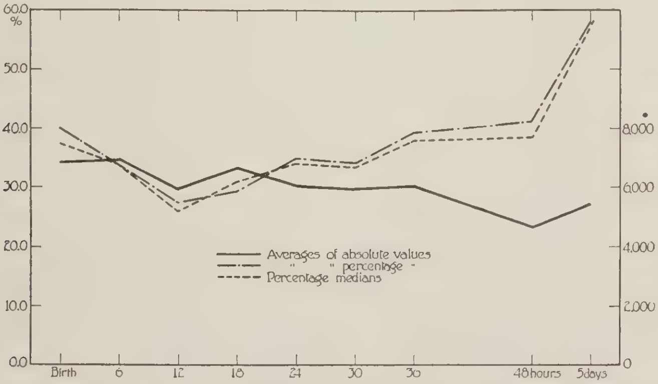

Fig. 18.—Absolute and percentage counts of medium sized lymphocytes.

TABLE 9.—*Absolute and Percentage Number of Medium Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	40.2 **6,841**	37.6 **6,278**	64.0 **15,392**	17.4 **2,896**	12.197 **3,148**	30.3 **46.01**	42
6	5 to 7	33.6 **6,921**	33.6 **6,753**	51.8 **12,864**	14.6 **1,081**	10.239 **2,871**	30.5 **41.49**	30
12	11 to 13	27.5 **5,967**	25.8 **5,358**	44.8 **10,841**	14.4 **1,012**	8.703 **2,380**	31.6 **39.88**	30
18	15 to 21	29.4 **6,635**	31.0 **6,665**	75.6 **19,504**	6.0 **1,764**	10.081 **2,365**	34.2 **35.64**	30
24	23 to 25	34.7 **6,083**	34.0 **5,880**	55.0 **11,615**	13.8 **2,691**	10.783 **2,568**	31.1 **42.22**	30
30	29 to 31	34.0 **5,984**	33.2 **5,525**	51.6 **11,248**	17.8 **2,775**	9.052 **2,034**	26.6 **33.99**	30
36	34 to 38	39.4 **6,018**	38.0 **6,423**	57.4 **7,996**	25.0 **2,856**	8.785 **1,567**	22.3 **26.04**	30
48	46 to 50	40.8 **4,634**	38.2 **4,593**	64.0 **7,568**	17.2 **1,462**	9.258 **1,434**	22.7 **30.94**	30
5 days		57.7 **5,459**	57.8 **5,220**	75.6 **8,321**	36.6 **2,457**	11.130 **1,434**	19.3 **26.26**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

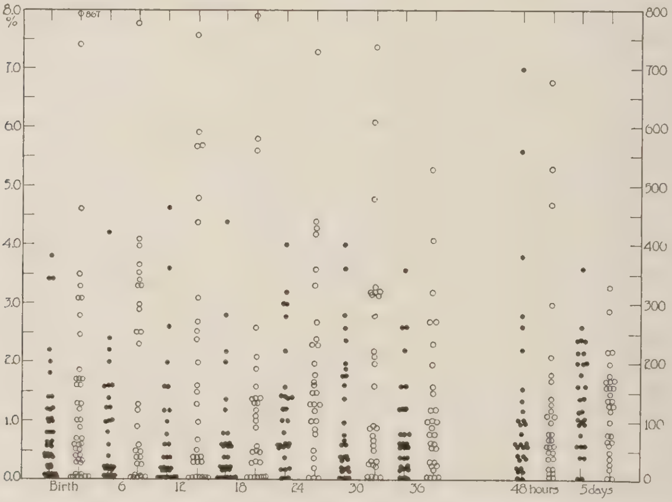

Fig. 19.—The distribution of absolute and percentage counts of large lymphocytes. Solid dots, percentage counts; circles, absolute counts.

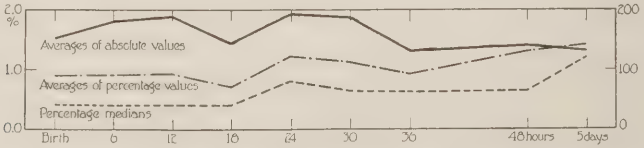

Fig. 20.—Absolute and percentage counts of large lymphocytes.

The medium lymphocytes usually form about from 85 to 90 per cent. of all the lymphocytes (Figs. 17 and 18 and Table 9, Figs. 19 and 20 and Table 10).

TABLE 10.—*Absolute and Percentage Number of Large Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.9 **151**	0.4 **91**	3.8 **867**	0.0 **0.0**	0.943 **184.86**	117.9 **122.42**	42
6	5 to 7	0.9 **179**	0.4 **121**	4.2 **777**	0.0 **0.0**	0.953 **183.74**	105.9 **102.65**	30
12	11 to 13	0.9 **189**	0.4 **108**	4.6 **759**	0.0 **0.0**	1.135 **215.92**	126.1 **114.24**	30
18	15 to 21	0.7 **141**	0.4 **100**	4.4 **792**	0.0 **0.0**	0.964 **184.76**	137.7 **131.04**	30
24	23 to 25	1.2 **193**	0.8 **151**	4.0 **729**	0.0 **0.0**	1.044 **160.10**	87.0 **82.95**	30
30	29 to 31	1.1 **187**	0.6 **95**	4.0 **738**	0.0 **0.0**	1.053 **176.59**	95.7 **94.43**	30
36	34 to 38	0.9 **128**	0.6 **99**	3.6 **530**	0.0 **0.0**	0.871 **125.91**	96.8 **98.37**	30
48	46 to 50	1.3 **137**	0.6 **87**	7.0 **679**	0.0 **0.0**	1.590 **158.96**	122.3 **116.03**	30
5 days		1.4 **131**	1.2 **140**	3.6 **331**	0.0 **0.0**	0.824 **77.75**	58.9 **59.35**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

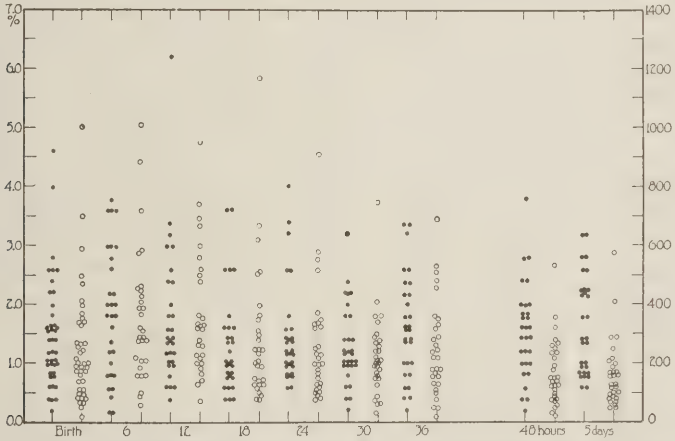

Fig. 21.—The distribution of absolute and percentage counts of mononuclear leukocytes. Solid dots, percentage counts; circles, absolute counts.

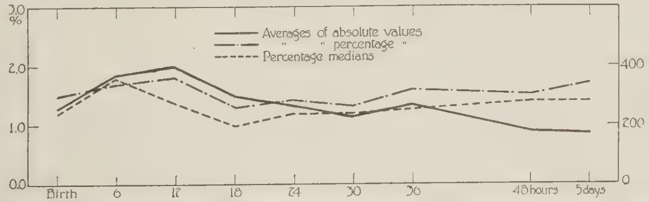

Fig. 22.—The absolute and percentage counts of mononuclear leukocytes.

(*e*) The Large Mononuclear Leukocytes: The curve of the large mononuclears is similar to that of the lymphocytes, and the variations at the various time intervals correspond closely to those of the total lymphocytes. The average of large mononuclears is usually about 1.5 per cent (Figs. 21 and 22 and Table 11).

TABLE 11.—*Absolute and Percentage Number of Large Mononuclear Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	1.5 **255**	1.2 **198**	4.6 **1,002**	0.2 **20**	0.911 **187.33**	60.73 **73.46**	42
6	5 to 7	1.7 **363**	1.8 **312**	3.8 **1,015**	0.2 **68**	0.905 **220.32**	53.24 **60.69**	30
12	11 to 13	1.8 **399**	1.4 **336**	3.4 **1,413**	0.4 **76**	1.153 **279.58**	64.06 **70.07**	30
18	15 to 21	1.3 **290**	1.0 **243**	3.6 **1,170**	0.4 **84**	0.793 **224.33**	61.00 **77.36**	30
24	23 to 25	1.4 **265**	1.2 **223**	4.0 **912**	0.6 **81**	0.836 **180.36**	59.71 **68.06**	30
30	29 to 31	1.3 **230**	1.2 **218**	3.1 **755**	0.2 **34**	0.655 **133.24**	50.38 **57.93**	30
36	34 to 38	1.6 **253**	1.6 **225**	3.4 **693**	0.2 **21**	0.842 **157.64**	52.62 **62.31**	30
48	46 to 50	1.5 **176**	1.4 **154**	3.8 **532**	0.2 **26**	0.781 **109.45**	52.07 **62.19**	30
5 days		1.7 **170**	1.4 **160**	3.2 **416**	0.6 **53**	0.818 **110.61**	48.12 **65.06**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

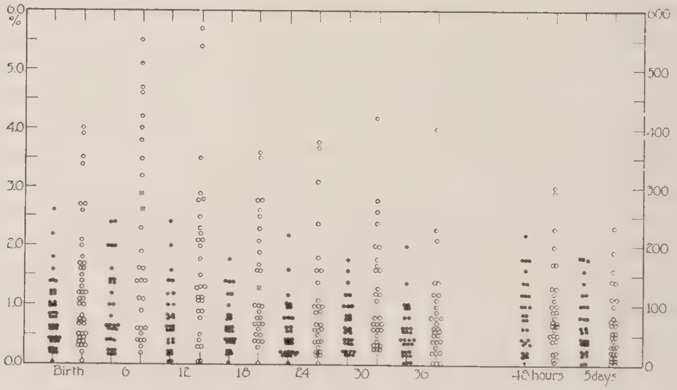

Fig. 23.—The distribution of the absolute and percentage counts of transitional leukocytes. Solid dots, percentage counts; circles, absolute counts.

(*f*) The Transitional Leukocytes: The transitionals are relatively uncommon. When the absolute values are plotted a curve results that closely resembles that of the P. M. N. neutrophils (Figs. 23 and 24 and Table 12).

(*g*) The Eosinophilic Leukocytes: The eosinophils, when plotted according to percentages, showed a very interesting curve. Immediately after birth there was a slight drop until twelve hours, followed by a continuous rise until forty-eight hours after birth. However, on plotting the absolute values it was seen that there was no true eosinophilia. The count increases slowly until thirty hours and then decreases. This is a further argument against drawing conclusions from percentage values only (Figs. 25 and 26 and Table 13). The highest eosinophil percentage observed was 7.2. In exceptional instances no eosinophils were seen.

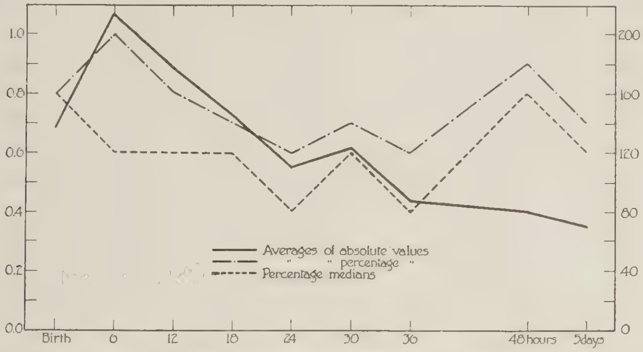

Fig. 24.—The absolute and percentage counts of transitional leukocytes.

TABLE 12.—*Absolute and Percentage Number of Transitional Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.8 **137**	0.8 **119**	2.6 **408**	0.0 **0.0**	0.547 **103.00**	68.4 **75.18**	42
6	5 to 7	1.0 **213**	0.6 **168**	2.4 **559**	0.2 **47**	0.678 **161.68**	67.8 **75.91**	30
12	11 to 13	0.8 **177**	0.6 **132**	2.4 **576**	0.0 **0.0**	0.556 **137.03**	69.5 **77.42**	30
18	15 to 21	0.7 **144**	0.6 **103**	1.8 **364**	0.0 **0.0**	0.435 **94.34**	62.1 **65.51**	30
24	23 to 25	0.6 **109**	0.4 **71**	2.2 **388**	0.0 **0.0**	0.447 **97.62**	74.5 **89.56**	30
30	29 to 31	0.7 **123**	0.6 **86**	1.8 **424**	0.2 **32**	0.424 **92.41**	60.6 **75.13**	30
36	34 to 38	0.6 **87**	0.4 **63**	2.0 **408**	0.0 **0.0**	0.424 **81.24**	70.7 **93.38**	30
48	46 to 50	0.9 **79**	0.8 **81**	2.2 **308**	0.0 **0.0**	0.583 **81.26**	64.8 **105.53**	30
5 days		0.7 **70**	0.6 **52**	1.8 **237**	0.0 **0.0**	0.519 **58.25**	74.1 **83.21**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*h*) The Eosinophilic Metamyelocytes: Eosinophilic metamyelocytes are rare. They are occasionally seen at from thirty to thirty-six hours after birth, when the number of eosinophils is greatest.

(*i*) The Eosinophilic Myelocytes: Eosinophilic myelocytes are still less frequent. Usually, when eosinophilic myelocytes are present, eosinophilic metamyelocytes can be found in the same smear.

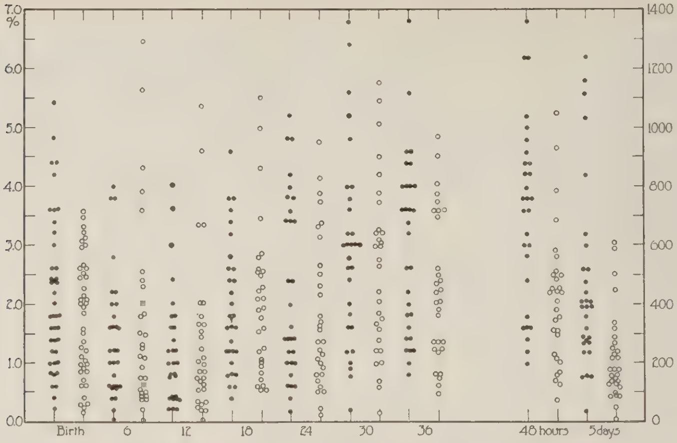

Fig. 25.—The distribution of the absolute and percentage counts of eosinophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

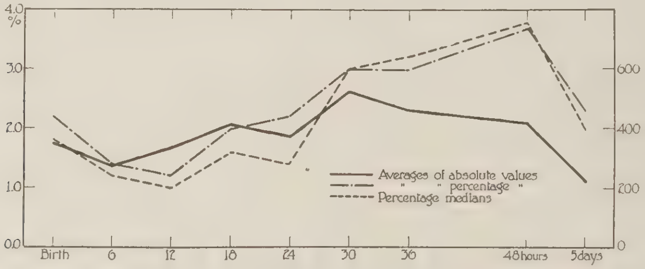

Fig. 26.—The absolute and percentage counts of eosinophilic leukocytes.

Table 13.—*Absolute and Percentage Number of Eosinophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	2.2 **356**	1.8 **392**	5.4 **716**	0.2 **37**	1.272 **199.21**	57.82 **55.96**	42
6	5 to 7	1.4 **272**	1.2 **192**	4.0 **1,076**	0.0 **0.0**	0.948 **304.50**	67.71 **92.27**	30
12	11 to 13	1.2 **330**	1.0 **256**	4.0 **1,292**	0.0 **40**	0.888 **254.62**	74.00 **93.61**	30
18	15 to 21	2.0 **410**	1.6 **393**	4.6 **1,108**	0.4 **110**	1.058 **251.26**	52.90 **61.28**	30
24	23 to 25	2.2 **371**	1.4 **319**	5.2 **955**	0.2 **29**	1 466 **253.24**	66.64 **68.26**	30
30	29 to 31	3.0 **525**	3.0 **553**	6.8 **1,152**	0.2 **30**	1.596 **289.97**	53.20 **55.23**	30
36	34 to 38	3.0 **462**	3.2 **448**	6.8 **975**	0.8 **126**	1.479 **247.49**	49.30 **53.57**	30
48	46 to 50	3.7 **419**	3.8 **442**	7.2 **1,051**	1.0 **89**	1.664 **228.68**	44.97 **54.58**	30
5 days		2.3 **221**	2.0 **182**	6.2 **616**	0.2 **13**	1.466 **148.01**	63.74 **66.97**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*j*) The Basophilic Leukocytes: Basophils are rarely seen in the blood of the new-born. At birth they are relatively numerous both in percentage and in absolute numbers. After birth they decrease (Figs. 27 and 28 and Table 14).

(*k*) The Rieder Cells: The Rieder cells are most numerous during the first twenty-four hours. Their numbers do not vary greatly and they seem to follow the curve of the lymphocytes. This is to be expected, since the Rieder cell seen in this study was limited to the lymphocyte type. At five days there is a slight increase in their frequency, corresponding to the increase in lymphocytes.

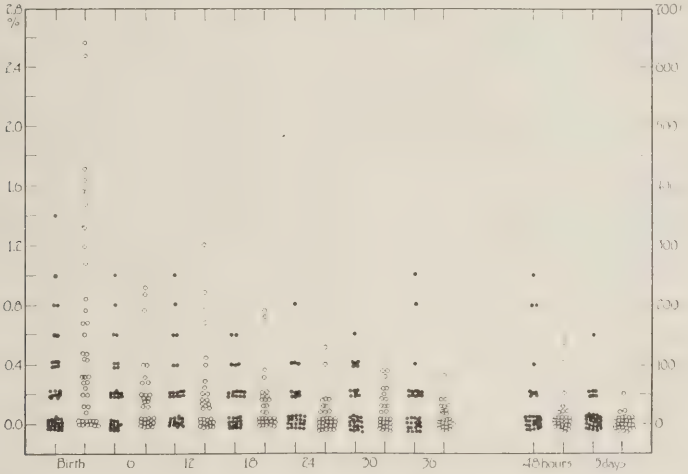

Fig. 27.—The distribution of the absolute and percentage counts of basophil leukocytes. Solid dots, percentage counts; circles, absolute counts.

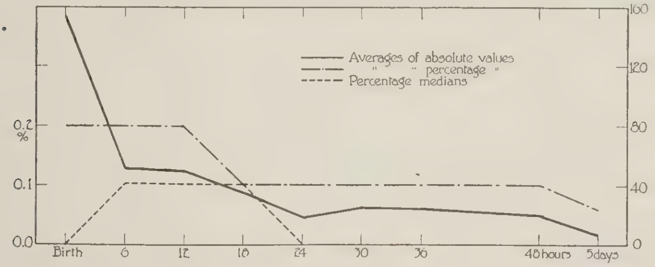

Fig. 28.—The absolute and percentage counts of basophil leukocytes.

(*l*) The Plasma Cells: The plasma cells are infrequent. Their number is slightly greater during the first day and they show a definite rise at the five day period.

(*m*) The "Unusual" Cells: The so-called "unusual" cell, having the character of both a P. M. N. neutrophil and a promyelocyte, occurs occasionally during the first twenty-four hours but rarely after this period. It apparently is a cell that belongs to the neutrophil series and represents an irritation type. Occasionally more than one is seen in the same smear, and in one case five were seen.

(*n*) The Türke's Cell: The Türke's cell is rare. Two were seen during the first twelve hours. Both were present during markedly increased lymphatic activity.

TABLE 14.—*Absolute and Percentage Number of Basophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.2 **153**	0.0 **80**	1.8 **642**	0.0 **0.0**	0.300 **179.38**	1.50 **117.8**	42
6	5 to 7	0.2 **50**	0.2 **42**	1.0 **233**	0.0 **0.0**	0.244 **64.55**	1.22 **129.1**	30
12	11 to 13	0.2 **48**	0.2 **30**	1.0 **300**	0.0 **0.0**	0.244 **71.76**	1.22 **149.5**	30
18	15 to 21	0.1 **34**	0.2 **24**	0.6 **195**	0.0 **0.0**	0.173 **49.59**	1.73 **145.8**	30
24	23 to 25	0.1 **17**	0.0 **0.0**	0.8 **137**	0.0 **0.0**	0.173 **32.06**	1.73 **188.6**	30
30	29 to 31	0.1 **23**	0.0 **0.0**	0.6 **94**	0.0 **0.0**	0.173 **30.25**	1.73 **131.5**	30
36	34 to 38	0.1 **24**	0.0 **0.0**	1.0 **184**	0.0 **0.0**	0.223 **45.84**	2.23 **191.0**	30
48	46 to 50	0.1 **19**	0.0 **0.0**	1.0 **144**	0.0 **0.0**	0.264 **38.65**	2.64 **214.7**	30
5 days		0.06 **6**	0.0 **0.0**	0.6 **55**	0.0 **0.0**	0.100 **12.25**	1.00 . **204.1**	30

* The upper figures represent percentage counts; the figures in bold face, the total counts.

(*o*) The Degeneration Forms: Broken cells would probably be a more appropriate name for this type. These have been very briefly mentioned in the literature, and a few investigators state that destroyed cells are often seen in the blood smears of the new-born. In this study an attempt has been made to classify the different types.

In general, there is a tendency for the cell count to be high when the number of degeneration forms is high. The curve in Figure 29 illustrates the close relationship between the total degeneration count and the total white count, as shown in Figure 7. The curve taken by the degenerate lymphocytes (Figs. 30 and 31 and Table 15) is very similar to that of the total lymphocyte count. With one or two exceptions the same applies for the neutrophil degeneration forms (Figs. 32 and 33 and Table 16).

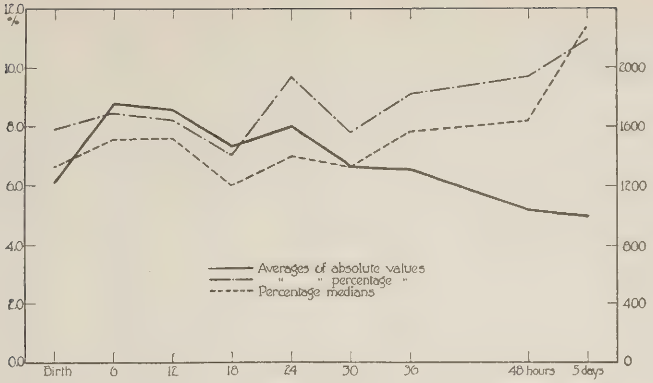

Fig. 29.—The absolute and percentage counts of all degenerating leukocytes.

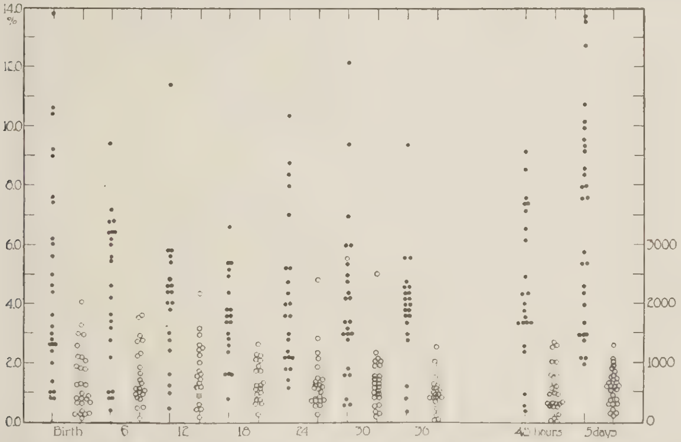

Fig. 30.—The distribution of the absolute and percentage counts of degenerating lymphocytes. Solid dots, percentage counts; circles, absolute counts.

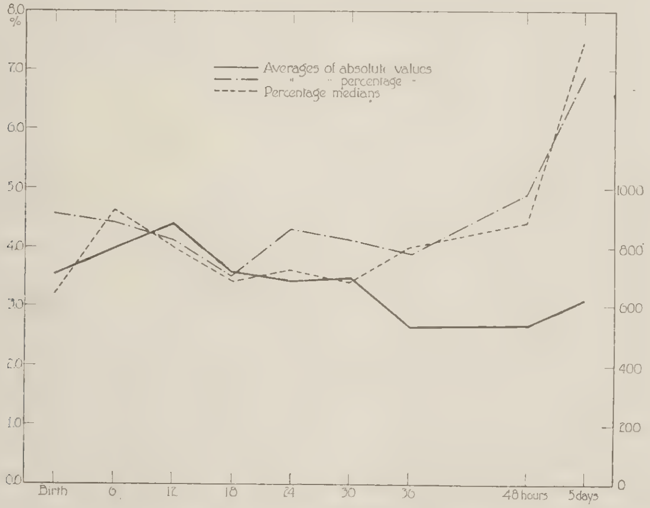

Fig. 31.—The absolute and percentage counts of degenerating lymphocytes.

TABLE 15.—*Absolute and Percentage Number of Degenerating Lymphocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	4.6 **709**	3.2 **612**	13.8 **2,014**	0.0 **110**	3.858 **521.02**	83.87 **73.49**	28
6	5 to 7	4.4 **792**	4.6 **604**	9.4 **1,849**	0.4 **50**	2.420 **548.14**	55.00 **59.78**	23
12	11 to 13	4.1 **878**	4.0 **777**	11.4 **2,188**	0.4 **82**	2.323 **506.98**	56.66 **57.74**	20
18	15 to 21	3.5 **706**	3.4 **588**	6.6 **1,325**	0.8 **144**	1.479 **323.11**	42.26 **45.77**	20
24	23 to 25	4.3 **687**	3.6 **600**	10.4 **2,412**	1.2 **135**	2.551 **478.92**	59.33 **69.71**	23
30	29 to 31	4.1 **692**	3.4 **615**	12.2 **2,513**	0.6 **103**	2.590 **466.48**	63.17 **67.41**	25
36	34 to 38	3.9 **530**	4.0 **507**	9.4 **1,269**	0.4 **54**	1.676 **288.92**	42.97 **54.51**	22
48	46 to 50	4.9 **540**	4.4 **494**	14.6 **1,324**	0.4 **46**	3.029 **358.94**	61.82 **66.47**	26
5 days		6.9 **620**	7.6 **621**	13.8 **1,346**	2.0 **162**	3.534 **284.44**	51.22 **45.88**	29

* The upper figures represent percentage counts; the figures in bold face, the total counts.

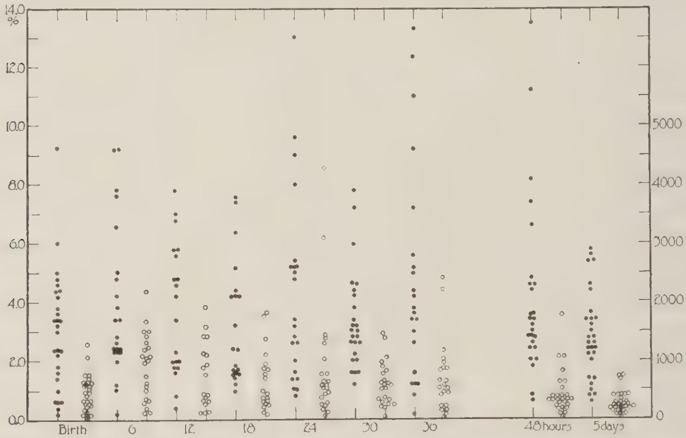

Fig. 32.—The distribution of absolute and percentage counts of degenerating neutrophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

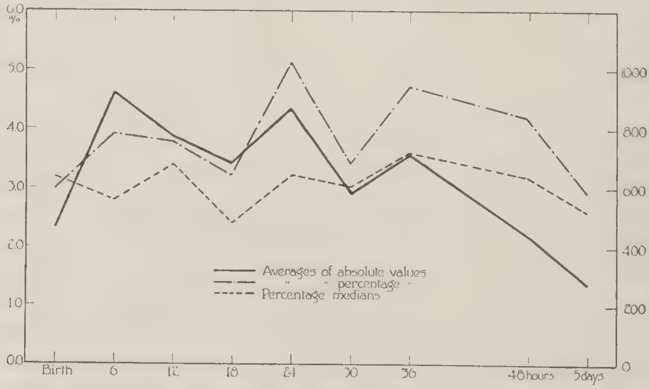

Fig. 33.—The absolute and percentage counts of degenerating neutrophilic leukocytes.

TABLE 16.—*Absolute and Percentage Number of Degenerated Neutrophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.0	3.2	9.2	0.2	1.959	65.3	28
		460	**414**	**1,269**	**35**	**298.17**	**64.8**	
6	5 to 7	3.9	2.8	9.2	0.2	2.501	64.1	23
		917	**1,036**	**2,190**	**100**	**480.51**	**60.7**	
12	11 to 13	3.8	3.4	7.8	0.4	2.179	57.3	20
		769	**782**	**1,938**	**123**	**547.44**	**71.2**	
18	15 to 21	3.2	2.4	7.6	1.0	2.128	66.5	20
		677	**424**	**1,831**	**108**	**504.57**	**74.6**	
24	23 to 25	5.1	3.2	23.0	0.8	4.919	96.5	23
		865	**598**	**4,278**	**75**	**956.39**	**110.6**	
30	29 to 31	3.4	3.0	7.8	1.2	1.685	45.5	25
		582	**516**	**1,483**	**45**	**353.97**	**60.8**	
36	34 to 38	4.7	3.6	13.4	0.2	3.674	78.2	22
		708	**589**	**2,430**	**28**	**601.42**	**85.0**	
48	46 to 50	4.2	3.2	13.6	0.6	2.969	70.7	26
		438	**316**	**1,768**	**40**	**368.10**	**84.0**	
5 days		2.9	2.6	5.8	0.6	1.466	50.6	29
		274	**246**	**739**	**55**	**176.97**	**64.6**	

* The upper figures represent percentage counts; the figures in bold face, the total counts.

In the case of the eosinophils, however, the curves of the total count of degeneration forms and the total number of normal cells do not correspond. As will be seen in Figures 34 and 35 and Table 17, the eosinophil degeneration is greatest at five days. There seems to be a gradual tendency toward increased degeneration throughout the period.

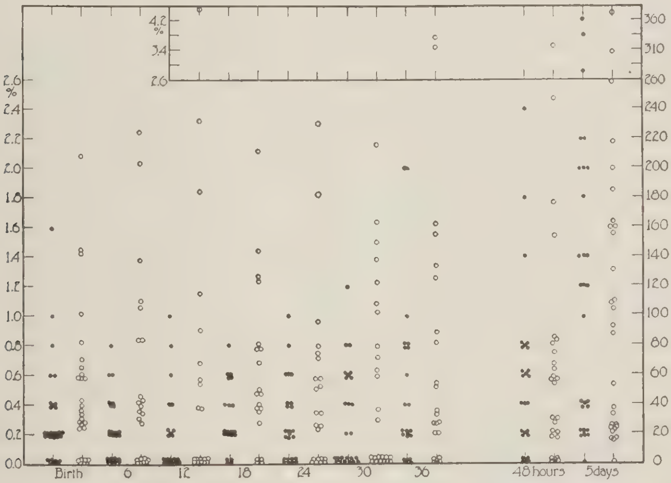

Fig. 34.—The distribution of absolute and percentage counts of degenerating eosinophilic leukocytes. Solid dots, percentage counts; circles, absolute counts.

(*p*) The Nucleated Red Blood Cells: Figures 36 and 37 and Table 18 show the incidence of the nucleated red blood cells. The number is greatest at birth, but between birth and eighteen hours there is a sudden decrease. The curve then flattens out until thirty hours and is followed by a gradual decrease for five days, when only one nucleated red cell was seen in the entire thirty cases.

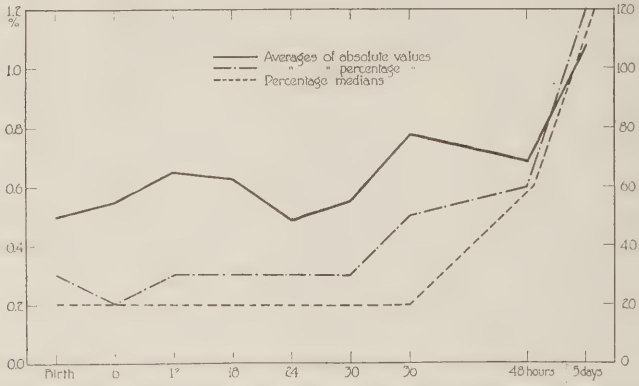

Fig. 35.—The absolute and percentage counts of degenerating eosinophilic leukocytes.

TABLE 17.—*Absolute and Percentage Number of Degenerated Eosinophil Leukocytes*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	0.3 **49**	0.2 **37**	1.6 **208**	0.0 **0.0**	0.346 **50.33**	115.3 **102.7**	28
6	5 to 7	0.2 **54**	0.2 **36**	0.8 **224**	0.0 **0.0**	0.223 **63.24**	111.5 **117.1**	23
12	11 to 13	0.3 **64**	0.2 **37**	1.0 **384**	0.0 **0.0**	0.479 **99.49**	159.7 **155.5**	20
18	15 to 21	0.3 **62**	0.2 **48**	0.8 **212**	0.0 **0.0**	0.223 **53.57**	74.3 **86.4**	20
24	23 to 25	0.3 **48**	0.2 **34**	1.0 **230**	0.0 **0.0**	0.264 **57.90**	88.0 **120.6**	23
30	29 to 31	0.3 **54**	0.2 **30**	1.2 **216**	0.0 **0.0**	0.331 **63.86**	110.3 **118.3**	25
36	34 to 38	0.5 **77**	0.2 **36**	2.0 **330**	0.0 **0.0**	0.565 **92.30**	113.0 **119.9**	22
48	46 to 50	0.6 **68**	0.6 **57**	2.5 **316**	0.0 **0.0**	0.663 **76.24**	110.5 **112.1**	26
5 days		1.2 **108**	1.2 **93**	4.2 **373**	0.0 **0.0**	1.086 **95.22**	90.5 **88.2**	29

* The upper figures represent percentage counts; the figures in bold face, the total counts.

In general, the nucleated red cells are slightly larger than the normal erythrocytes. Practically all are polychromatophilic, i. e., they belong to Group II or IV. Nucleated cells of Type I and III, i. e., with red cytoplasm, usually appear when large numbers of nucleated red cells are present. In these cases the large forms of nucleated red blood cells are also quite commonly seen.

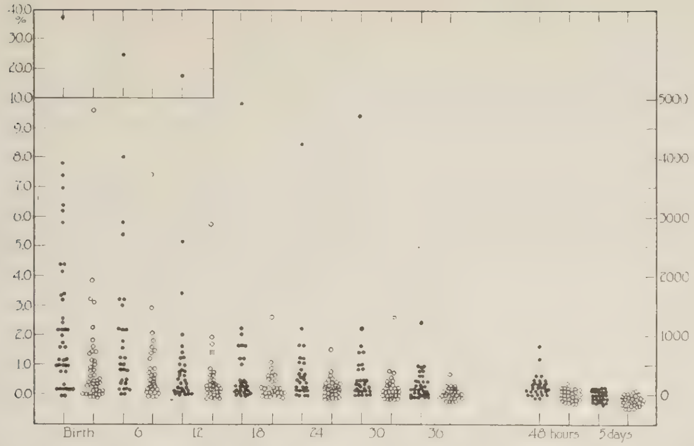

Fig. 36.—The distribution of the absolute and percentage counts of nucleated red blood corpuscles. Solid dots, percentage counts; circles, absolute counts.

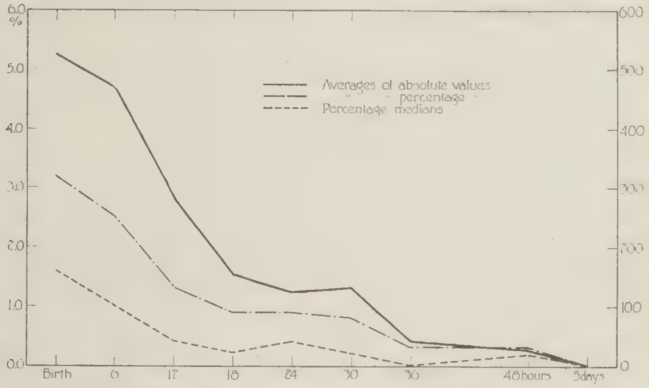

Fig. 37.—The absolute and percentage counts of nucleated red blood cells.

TABLE 18.—*Nucleated Red Blood Corpuscles Per 100 White Blood Corpuscles and Per Cubic Millimeter*

Age (Hours)		Total and Percentage Values*						Number of Cases
Median	Range	Average	Median	Maximum	Minimum	Standard Deviation	Coefficient of Variability	
0.5	0 to 1.5	3.2	1.6	37.8	0.0	5.818	181.81	42
		523	**492**	**4,800**	**0.0**	**665.82**	**127.3**	
6	5 to 7	2.5	1.0	24.4	0.0	12.715	508.6	30
		469	**250**	**3,708**	**0.0**	**697.57**	**148.7**	
12	11 to 13	1.3	0.4	17.8	0.0	3.249	249.9	30
		277	**70**	**2,883**	**0.0**	**546.02**	**197.1**	
18	15 to 21 †	0.9	0.2	9.8	0.0	1.783	198.1	30
		152	**48**	**1,274**	**0.0**	**249.31**	**164.0**	
24	23 to 25	0.9	0.4	8.4	0.0	1.506	167.3	30
		122	**46**	**756**	**0.0**	**151.41**	**124.1**	
30	29 to 31	0.8	0.2	9.4	0.0	1.700	212.5	30
		130	**43**	**1,616**	**0.0**	**292.92**	**225.3**	
36	34 to 38 †	0.3	0.0	2.4	0.0	0.469	156.3	30
		39	**0**	**324**	**0.0**	**66.89**	**171.5**	
48	46 to 50 †	0.3	0.2	1.6	0.0	0.360	120.0	30
		26	**14**	**152**	**0.0**	**36.45**	**140.2**	
5 days		0.0	0.0	0.2	0.0			
		0	**0**	**22**	**0.0**			

* The upper figures represent percentage counts; the figures in bold face, the total counts.

† 15 to 21 hours, only one case at 15 and one at 21 hours; 34 to 38 hours, only one case at 34 and one at 38 hours; 46 to 50 hours, two cases at 46 and two at 50 hours.

In only one case were there no nucleated red cells encountered at birth. In this instance one nucleated red cell was seen in a smear taken thirteen hours after birth, one at twenty-five hours and none at thirty-six or fifty hours.

Apparently the amount of polychromatophilia varies directly with the number of nucleated red cells. Thus in Case 4, in which no nucleated red blood cells were noted at 6, 12, 18 and 31 hours, there was little polychromatophilia until at forty-six hours when it became definitely noticeable, and two nucleated red cells were observed.

Case 25 was very unusual. At birth there were 37.8 nucleated red cells for every 100 leukocytes. This infant was born at term and weighed 3,690 gm. (8 pounds). After birth the number of nucleated red cells decreased rapidly and at thirty hours there were 9.4 for every 100 leukocytes. No nucleated red cells were present in the blood smears at five days. Other evidences of an increased red cell production were present. There were many naked erythroblast nuclei (Fig. 1 *r*), and all sizes of nucleated red cells including microblasts and megaloblasts. Mitotic figures were present at seven and eleven hours. The nuclei of many of the red cells were divided into three or four lobes and some contained Howell-Jolly bodies. No basophilic punctation could be found. Despite all the evidence of increased erythrogenesis in this case, the red count remained comparatively low, being below five million per cubic millimeter, except in one instance when it reached five million.

Apparently red cell formation does not vary with neutrophil production. Very often when there is evidence of hyperactivity of the red cells, the reverse is true of the neutrophils.

The shadows of red blood cells are not more commonly seen in new-born blood than in that of the normal adult.

As previously noted by other observers, rouleaux formation is not as active in new-born as in adult blood.

Polychromatophilia is as common in the average sized red cell as in the larger ones. The degree of polychromatophilia is quite variable (Fig. 1 *s*).

Poikilocytosis was observed repeatedly. Unlike the large pear-shaped cells seen in severe anemias, these cells are small and often pale (Fig. 1 *s*). In addition, one often sees small irregular red masses which seem to be detached portions of other red cells. The smallest microcytes are present in new-born blood, especially when red cell production is hyperactive.

Anisocytosis, which is seen in every smear, persists definitely at five days. At this time poikilocytosis and polychromatophilia are rare.

(*q*) Platelets: As a rule the platelets seem more variable in size than those seen in the adult, and forms larger than normal are rather common (Fig. 1 *t*). The granulation was in no way peculiar.

5. *The Leukocyte Granules.*—The neutrophilic and eosinophilic granules are similar to those of the normal adult in every respect. The azure granulation tends to be less abundant than in the normal adult. However, the variations are similar, so that on one day the granules may be abundant, while on the next they may be scanty.

6. *Icterus Neonatorum.*—In this work it was possible, by examining the blood at different intervals, to determine whether blood changes took place during the development of marked icterus. In the few cases of marked icterus the blood showed no abnormalities. One case showed a very low eosinophil count, 0.2 per cent. at six days, but in the other cases the eosinophils were normal.

7. *Sex Differences.*—No difference in the blood findings of newborn males and females were noted in the present study.

8. *Numerical and Graphical Results.*—Although a very large number of individual and serial counts of the various types of blood cells for all periods of postnatal life have been published, the only attempts to estimate the variability of these counts were given in the form of estimates of the range, as indicated by the maxima and minima. While the range is one of the commonest measures of deviation used in the study of variable observations, it is perhaps the least valuable of all the measures which have been devised for the purpose. Among the objections which may be raised to its exclusive use are the following: First, it is dependent on two observations only, the largest and smallest of the series, and it can be no more accurate than these observations; Second, it is little influenced by the number of observations in the series, the range on 200 cases being as liable to vary as the range in a series of two cases. Third, it gives no concept of the relation of the individual observations to the average of these observations, for the maximal and minimal observations may be far removed from the average, while the great majority of the observations are closely clustered about the average. It seems highly desirable that modern measures of dispersion should be applied to blood counts at all ages, since the variations in these counts are used constantly for differentiating the normal from the abnormal, as well as for the study of changes under different physiologic conditions.

The study of the variability of the various blood counts in the newborn has been carried out by the computation of the standard deviation and the coefficients of variability, as explained in the section on statistical methods in the foregoing part of this paper. In the present section, a brief summary will be given of the results obtained with these methods.

The variability of the red blood corpuscles was determined on the basis of a unit of 10,000 cells, since the original counts were made to this figure. The deviations of the various individual counts from the median and average are shown in Figure 3, and the calculated deviations are fairly symmetrical, as shown by the close relation of the median to the average count. The average range of the cases is about 2.5 million. The range seems to be greater in the middle of the period of observation than at the beginning or at the end. The standard deviation ranges from about 500,000 to about 750,000. It is greatest between the sixth and twenty-fourth hours. Taken as a whole, the coefficient of variability of the red blood cell count is remarkably small and very constant. It averages about 11 per cent. How constant the red blood count of the new-born really is may be shown by comparing its coefficient of variability with that of some other measures in the new-born; thus the variability in height at birth is about 6 per cent., the variability in weight is about 15 per cent., while the variability in weight of the thymus is 47 per cent., and that of the weight of the thyroid is 53 per cent. There is no evidence that the coefficient of variability of the red cell count changes with the increase in this count in the course of the first day.

In contrast to the red blood cells, the blood platelet count is very variable. The range between the maximal and minimal counts runs between 200,000 and 400,000. The distribution of the cases tends toward the minimum, as is indicated by a median which is always lower than the arithmetic average. The standard of deviation averages about 65,000 and the coefficient of variability ranges from 46.1 to 28.5 per cent. There is a very distinct drop in the variability after the first day.

While the variability of the total white cell count is relatively larger than that of the red cell count, it is fairly constant when one considers the different factors which may affect it. The range of variation, however, is very great, being over 10,000. On the average, the standard deviation varies from 5.26 thousand at thirty hours to 2.52 thousand on the fifth day. The coefficient of variability is about 25 per cent. of the average. It is greatest at birth, but from six hours on throughout the period of observation it is quite constant.

The variability of the absolute counts of the various types of white blood cells differs greatly with the several varieties.

The polymorphonuclear leukocytes have an average range of over 15,000, and the average of the standard deviations is, in round numbers, about 3,000. The coefficient of variability is about 35 per cent. of the average count. Thus the polymorphonuclear leukocyte count is about one-third more variable than that of the total white cell count. There is no consistant change in the variability of the total absolute number of the polymorphonuclear leukocytes during the period of observation.

The range in total number of the lymphocyte cells averages about 7,000, and the standard deviation declines from about 3,500 at birth to about 1,500 at the end of the period of observation. The coefficient of variability ranges from 46.5 at birth to 25.0 per cent. at five days after birth. Both the standard deviation and the coefficient of variability drop steadily and consistently after the first day, although there is only a slight decrease in the actual count of lymphocytes in this period.

The changes in the variability of the medium sized lymphocytes is practically the same as that in the entire lymphocyte group, since they form the greater part of this group.

Both the large and the small lymphocytes show the greatest variability. In the case of the former the coefficient of variability ranges from 122.4 per cent. at birth to 59.3 per cent. at five days. In the latter, the coefficient of variability shows no constant change except that it is lower on the fifth day than earlier.

The range of the absolute number of large mononuclear leukocytes is extremely great, being on the average about 1,000, while the average absolute count is about 250. It shows no great or consistent change during the period of observation.

The variation of the transitional leukocytes is slightly greater than that of the large mononuclears, but like the latter shows no constant changes.

The eosinophil leukocytes are less variable than most of the cells which occur in small numbers in the circulating blood. While the range of variation is great, considering the small absolute number of cells, the coefficient of variability ranges from about 94 to 53 per cent. The variability is higher the first day than later.

The basophil leukocytes are the most variable of all the blood cells. The range of distribution is commonly about four times the average count in the period of observation, and the coefficient of variability has a minimum of 117.2 at birth and a maximum of 214.7 on the second day. Unlike most of the other cell counts the basophils become much more variable in the latter part of the period of observation.

The variability of the degenerated forms of leukocytes is not as great as might be expected from the nature of the material. The degenerated neutrophil leukocytes show an average coefficient of variability of about 80 per cent. At the end and the beginning of the period the coefficient is but little over 60 per cent., but it rises to over 100 per cent. at the end of the first day. The coefficient of variability of the degenerated eosinophils is higher than that of the neutrophils, averaging over 100 per cent. It is extremely irregular in the different intervals of observation.

The degenerating neutrophils show an average coefficient of variability of about 85 per cent. with no constant change.

The degenerating eosinophils show even a higher coefficient of variability, averaging about 90 per cent. The variability is quite irregular in the period of observation.

The variability of the degenerating lymphocytes is somewhat less, being about 60 per cent. It is higher at birth than at any other time in the period of observation.

The variability of the nucleated red corpuscles is very great. It ranges from 120 to 508 per cent. It shows no constancy at the various times of observation.

The percentage counts of the various leukocytes, taken as a whole, are much less variable than the absolute counts. The average coefficient of variability of the number of these cells is approximately 20 per cent. It shows no constant change during the period of observation. The variability of the number of lymphocytes is slightly greater than that of the polymorphonuclear leukocytes, averaging about 22 per cent. There is a distinct decrease in the variability after the first day. The variability of the large and small lymphocytes is very great, the coefficient of variability of the percentage count being almost or quite equal to that of the absolute count. The coefficient of variability of the large mononuclear lymphocytes averages about 55 per cent. The variability decreases somewhat after the first day. The coefficient of variability of the transitional leukocytes is somewhat greater than the large mononuclears, being between 65 and 70 per cent. The variability shows no consistent change during the period of observation. The count of the eosinophils shows an average coefficient of variability of about 55 per cent. It shows no constant change in the period. The percentage count of the basophils, like the absolute number of these cells, is tremendously variable. The average coefficient is approximately 170 per cent. Like the variability of the absolute numbers, the variability of the percentage count tends to increase during the new-born period. The coefficient of variability of the absolute number of lymphocytes is about 55 per cent. It is lower in the latter part of the period of observation than in the earlier. The absolute number of nucleated red blood corpuscles is extremely variable. The coefficient ranges from 127 on the first day to 225 per cent. at thirty hours.

COMMENT

1. *The Red Blood Cell Count.*—The rapid rise in the erythrocyte count during the first six hours explains the types of red cells observed. At this stage, nucleated red cells, polychromatophilia, anicocytosis and poikilocytosis are most frequently seen. After this initial stimulation the number of red blood cells decreases and tends to become fairly constant. If blood concentration is responsible for this rise in cell count,

surely the small intake of fluid between six and eighteen hours cannot restore conditions to normal. An analysis of our material shows definitely that the amount of weight loss in the first two days bears no relationship to the red cell count. Many of our cases were given complementary feedings of breast milk or lactose solution in an attempt to prevent the initial drop of weight. We were fortunate in obtaining several infants in whom the weight loss was very small. In these infants there was apparently very little concentration, and yet the rise in the red blood cell count was present. In only eight of the thirty-five cases studied, did the curves show an increase in red cells corresponding to the weight loss, while in fifteen cases the reverse was true.

At birth, the excretions are already formed in the bowel and bladder, and any concentration as a result of these excretions has already taken place. Further concentration would only occur if more of the excretions were rapidly formed, which is not the case in the first twelve hours. The amount of moisture lost in respiration during the first six hours apparently does not exceed that lost during the next twelve hours, so that there should be little change in blood concentration at different periods during the first eighteen hours because of fluid lost in respiration.

As will be shown later, the bone marrow is exceedingly active during the first few hours after birth, and this is probably an important factor in causing the initial rise in red cell count. Stimulation of any organ may be temporary, especially immediately after birth when such marked changes occur in the infant's organism.

It would be interesting to determine the blood volume of the newborn at the intervals studied in this work and to compare the results with our figures, for then one could state with absolute certainty whether or not concentration is a factor that helps to account for the initial increase of red blood cells.

2. *The Platelet Count.*—It is surprising that the neonatal rise, which is characteristic of the red and white cells, does not occur in the platelets; on the contrary the number begins to decline directly after birth. Lucas and his co-workers found no count less than 100,000, but in our series there were a few below this figure.

3. *The Leukocyte Count.*—The rapid rise and fall of the white cell count seems to be very uniform. The flattening of the curve between twenty-four and thirty hours is apparently due to the few unusually low counts at twenty-four hours. From forty-eight hours to five days the drop is slower. After the five day period other observers have found that the white count remains about from 7,000 to 10,000. This is mentioned chiefly because one often reads that increased leukocyte counts of 12,000 to 15,000 are normal values for infants and children.

4. *The Differential Leukocyte Count.*—The close relationship of the total leukocyte count to that of the polymorphonuclears indicates that the changing number of the latter is chiefly responsible for the variation in the white blood count during the first two days.

The metamyelocytes are irritation types of cells. In the normal differential count one may find one or two metamyelocytes in every 100 cells. In cases of leukocytosis as the result of inflammation, which we know is an expression of increased bone marrow activity, many metamyelocytes are seen. It is logical to assume, therefore, from the curve of the metamyelocytes that the bone marrow is in a state of hyperactivity during the first twelve to eighteen hours. In order to obtain a satisfactory idea of the neutrophilic components of the blood stream, it is necessary to add the values obtained for the neutrophilic metamyelocytes and polymorphonuclears.

The presence of neutrophilic myelocytes is another indication of stimulation of bone marrow activity. According to Pappenheim, one finds metamyelocytes and myelocytes in cases of bone marrow irritation, as in reaction to hemorrhage. Cells earlier than myelocytes occur only in pathologic reaction of the bone marrow.

The lymphocyte curve shows several points of interest. The literature contains a number of such curves representing percentage counts, and these indicate that during the first few days the number of lymphocytes gradually increases. That this is not the case is shown by the curve of the absolute number of cells.

When one studies the lymphocytes in the first twelve to eighteen hours, it is seen that here too, there are evidences of increased activity of lymphocyte production. For example, one sees earlier types of lymphocytes, cells with sieve-like nuclear structure. Other evidences of lymphocyte irritation will be shown later. When the number of total lymphocytes is high, one usually finds that the increase in the small and large forms is relatively greater than the increase of medium sized cells.

In this study, the absolute values of lymphocytes and polymorphonuclears were found to be equal at forty-eight hours, and after this period the lymphocytes were more numerous than the neutrophils. Practically all other observers have found that this change occurs between the fourth and sixth days.

The values of the mononuclears and transitionals closely approximate those of the normal adult. No cases were met in which the number of either of these cells was unusually high.

It is difficult to say whether any significance can be attached to the elevation in the number of eosinophils at thirty hours, but one infers that the eosinophil production is increased at this time since the total leukocyte count has dropped definitely at thirty hours.

In several of the smears eosinophils were noted in which the eosinophilic granules were embedded in a blue cytoplasm. Ordinarily, the cytoplasm consists entirely of these large coarse granules, the blue cytoplasm being present only in the earlier stages of eosinophil formation. This has been shown to be the case by Downey [37] in a study of eosinophil production in the marrow of the guinea-pig. It is possible that the same changes do not occur in man.

The presence of eosinophilic metamyelocytes and myelocytes is another evidence of bone marrow hyperactivity. Both are rarely seen; the metamyelocytes are more numerous.

. As others have shown basophils are rare in new-born blood, but there seems to be no previous record that the incidence is higher at birth. Although the numbers dealt with are small, still at birth there are three times as many basophils present as at twelve hours.

The Rieder cell is a distinct irritation type of cell seen only in increased hemopoietic activity. The lymphocytic type is more commonly met than the myeloid type and is frequently seen in Hodgkin's disease, lymphosarcoma and lymphatic leukemia. Its presence in this study is definite evidence of increased blood cell production.

Plasma cells are rarely seen in blood smears except when there is either lymphatic hyperactivity, or in chronic infectious diseases. The close relationship between lymphocyte and plasma cell formation has been definitely established.

The "unusual" cell or promyelocyte type is another evidence of a hyperactive blood forming mechanism. At first sight it seemed that this cell was typical of new-born blood, but later studies indicate that this is not the case.

Apparently no systematic study has previously been made of degeneration forms in human blood. It was found that these cells could be classified in groups and their curves of incidence determined. The close relationship between the total number of leukocytes and the number of degeneration forms suggests that they are more vulnerable during periods of the increased production of cells. One often sees degenerating lymphocytes in lymphatic leukemia and occasionally when lymphatic hyperplasia occurs, as in Hodgkin's disease. Apparently in these cases also, vulnerable cells are formed with rapid production.

Some cases show the tendency to produce more degenerate forms than others. In a few cases the number of degenerate forms at each successive time interval was increased.

Pressure in making the smears cannot be the cause of the increased degeneration in the first twelve hours, for the same technic was used at

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37. Downey, H.: The Origin and Development of Eosinophil Leukocytes and of Haematogenous Mast Cells in the Bone Marrow of Adult Guinea-Pig, Folia Haematol. **19**:148, 1915.

twelve hours as at five days, and unless the cells happened to be less resistant at twelve hours, there should be equal numbers of degenerate forms at both intervals. Furthermore, when studying the smears, one often sees several intact cells in the midst of a group of degeneration forms. Apparently the area under observation had been subjected to the same pressure throughout, and these cells, which were more vulnerable for a cause not specifically known, were more easily crushed.

As has been previously mentioned the eosinophil degeneration continues to increase from forty-eight hours to five days. The increase seen between forty-eight hours and five days corresponds to the increase in eosinophil count during the same period (Fig. 26). Apparently the vulnerability of the eosinophils occurs later than does that of the neutrophils and lymphocytes.

In a previous research on azure granulation,[38] an experiment was performed in which citrated blood was allowed to stand in a test tube on ice for several days. Smears were made every day, and it was noted that the eosinophils remained intact much longer than did the neutrophils and lymphocytes. In one case in the present study (Case 38 F) there were at five days nineteen degenerated eosinophils, ten degenerated neutrophils and ten degenerated lymphocytes to every 500 normal leukocytes. When one considers that the eosinophils formed but 6.2 per cent. of the total number of cells it is apparent that the degeneration was due to an increased vulnerability of that particular cell.

Nucleated red blood cells were found in every case studied. The total number does not increase from birth to twelve hours, as do most of the leukocytes.

The case cited in which the new-born had 37.8 per cent. nucleated red blood cells is very striking. One would think that either the marked reaction was pathologic or that prematurity was the causative factor. However, the child was definitely mature, and there was no clinical evidence present indicating any abnormality. The low erythrocyte count in the case suggests that an attempt was being made to produce red cells for the physiologic need.

The work of Drinker and Lund [39] helps to throw some light on our problem. They found in their perfusion experiments that when normal bone marrow is perfused under pressure, the marrow remains intact. When, however, the bone marrow is hyperactive and is sending out nucleated red blood cells, an increase of the blood supply will cause an increase in the number of nucleated red blood cells forced out into the circulation. It is very likely that the great variations observed in the numbers of nucleated red blood cells in our study were due to differences in the blood volumes of the new-born. Incidentally, early forms of lymphocytes and neutrophils are present in the case under discussion, so that in all likelihood the blood picture represents a normal new-born with an extremely hyperactive hemopoietic system.

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[38] Lippman, H. S.: A Comparative Study of Azure Granules Under Normal and Pathological Conditions, Mss., M. A. Thesis, University of Minnesota, 1920.

[39] Drinker, C. K.; Drinker, K. R., and Lund, C. C.: Circulation in Mammalian Bone Marrow, Am. J. Physiol. **62:**1 (Sept.) 1922

In most instances, no direct relationship exists between red cell and neutrophil cell formation. In fact, in numerous instances when red cell activity is markedly increased the neutrophil production is diminished.

The presence of megaloblasts and mitotic figures is indisputable evidence of an hyperactive bone marrow. In no case was basophilic stippling observed.

Taken as a whole, the red cell picture resembles that of secondary anemia following hemorrhage where one sees anisocytosis, polychromatophilia and nucleated reds. However, there is nothing present in the picture of the new-born blood to suggest anything but a physiologic process.

5. *The Leukocyte Granules.*—There is nothing unusual in the neutrophilic and eosinophilic granulation. The azure granules seem to be definitely reduced. The arrangements of the granules were found to be varied. Only a few of the smears contained cells with large coarse granules arranged in clumps and rows. They tend to be few in number, and medium or fine in size.

6. *The Causes of the Leukocytosis of the New-Born.*—In this series, infants whose delivery was attended by severe trauma showed leukocyte counts which corresponded closely to the averages for the entire group, so it does not seem probable that trauma is a factor in causing the leukocytosis of the new-born.

The theory of the causation of the natal leukocytosis through the peripheral stagnation of blood in the capillaries is not supported by this set of observations. The various components of the blood should all be quite similarly affected if the changes were simply due to a stagnation of cells. As a matter of fact, there is little relationship in each individual case between the number of red cells, platelets and leukocytes at the different time intervals. Again, the differential count should remain about the same at the various periods and this is not the case. The neutrophil reaction has been shown to be the cause of the fluctuating white cell count in the new-born child, the lymphocytes showing little change.

The concentration theory has been previously discussed. No special study was made of the effect of protein digestion on the new-born blood, but so far as could be determined the changes in the leukocyte count exhibited no relationship to the food ingested. The amount of food ingested during the first forty-eight hours is very slight, and the interval between feedings is too short to determine the effect of protein digestion with accuracy.

There are many facts that cannot be satisfactorily explained on the theory that the condition of the blood of the new-born is a result of the continuation of fetal blood formation. One cannot account for the rise in blood elements at twelve hours, for the high values, if due to fetal activity, should be present at birth, but this is not characteristic of the blood at birth. The morphology of the blood at birth approximates that of the last part of fetal life, and the picture presented is far different from that seen at six hours and again at twelve hours.

On the whole, the observations reported in this study support the view that the neonatal changes in the morphology of the blood are due to the increased stimulation of the blood forming organs, rather than to any of the factors just discussed.

SUMMARY

1. The morphology of the blood of the new-born differs in many respects from that of the adult. The present study was undertaken to fill a gap in the knowledge of new-born blood during the first forty-eight hours after birth. So many changes occur at this time that a careful analysis of these variations is essential. The forty-eight hour period, therefore, has been divided into eight parts, thirty cases being included in each interval. Counts were made of the red blood cells, leukocytes and platelets. Differential studies included the examination of 500 cells in each blood smear. White counts and differential studies were again made at five days, to secure a further check on the material.

2. The red blood cells at birth average 5.2 million per cubic millimeter. During the first six hours the count rises to 5.6 million. Following this there is a drop to 5.4 million at eighteen hours, after which time the count remains fairly constant until forty-eight hours after birth.

3. The platelet counts at birth average 213,000 per cubic millimeter. It drops to 170,000 during the first six hours. The decrease continues until 18 hours after birth and is then followed by a slight increase. No changes from normal were observed in the platelet counts in icterus neonatorum.

4. The total leukocyte count at birth averages 16,600 per cubic millimeter. At twelve hours it is 22,500, after which it gradually drops to 11,300 at forty-eight hours. At five days it has decreased to 9,500.

5. The differential counts show wide variations. The averages present curves which are often quite different from those reported in the literature. One of the striking features observed was the marked changes which may take place within a very few hours. In one instance the white count jumped from 25,000 to 34,000, while the P. M. N.'s

increased from 38 to 61 per cent. within six hours. It is important in any differential blood study to determine the absolute cell counts as well as the percentages. The curves often differ from each other to a great extent.

6. The P. M. N. neutrophils follow closely the total white count, and are primarily responsible for the leukocyte curve in the new-born period.

7. The neutrophilic metamyelocytes are very numerous in new-born blood. Values as high as 43 per cent. have been observed in this study. Our findings agree closely with those of Arneth on nuclear lobes in the neutrophils. Neutrophilic myelocytes are infrequent in new-born blood; they are most numerous during the first eighteen hours.

8. The absolute values of the lymphocytes vary little during the first five days. At birth and six hours after they are most numerous. There is a slight drop at twelve hours followed by a fairly constant number until forty-eight hours after birth. Between forty-eight hours and five days there is a moderate increase. The percentages show a definite increase in values from twelve hours to five days. The curves taken by the small, medium and larger lymphocytes are quite similar to the curve of the total lymphocytes.

9. The leukocytoid mesolymphocyte is not so commonly seen as is the large lymphocyte. The small lymphocytes are more numerous than the large. Whenever an absolute lymphocytosis occurs, the relative number of small and large lymphocytes is increased at the expense of the medium sized ones. Early forms of lymphocytes are quite common in the first twelve hours of life.

10. The relative and absolute values of lymphocytes and neutrophils are equal at forty-eight hours. After this time the values for the lymphocytes increase while those of the neutrophils decrease.

11. The mononuclears and transitionals are present in the same percentages as later in life. Both are more numerous during the first few hours.

12. The eosinophils gradually rise in number until thirty hours after birth and then become less numerous. The percentage curve shows an increase up to forty-eight hours. Eosinophilic metamyelocytes are occasionally seen. They are commonest at from thirty to thirty-six hours when the adult eosinophils are most numerous. They never form more than 0.4 per cent. of the cells.

13. Basophils are rare in new-born blood; they are most numerous at birth.

14. The Rieder cell is most frequently seen during the first twenty-four hours.

15. The plasma cell is rarely seen until five days after birth when it occasionally is present.

16. The "unusual" cell, or atypical neutrophilic promyelocyte, occurs occasionally during the first twenty-four hours, but rarely thereafter.

17. The frequency of degeneration forms of leukocytes in general varies directly with the total white count. They have been divided into three groups. The lymphocyte and neutrophil forms closely follow the curves of their respective types. In the case of the eosinophils, degeneration increases between forty-eight hours and five days, despite the fact that the eosinophil count diminishes during this period. The degeneration is probably due to an increased vulnerability of the leukocytes as a result of their overproduction during the first few days of life.

18. The nucleated red blood cells have been divided into four groups. In two groups the nuclei have a definite structure. The cytoplasm in one is acidophilic, in the other polychromatophilic. In this series of cases polychromatophilic nucleated red cells were much more commonly seen than those with acidophilic cytoplasm. The latter appeared only when there was marked increase in erythroblast formation, at which time microblasts, megaloblasts and even mitotic figures were seen. Naked red cell nuclei without cytoplasm were frequently seen when many nucleated red cells were present.

Every case studied showed nucleated red blood cells. At forty-eight hours about 50 per cent. had them, while at five days only one case showed one normoblast.

19. Normal new-born blood shows a lesser tendency to rouleaux formation than does normal adult blood. Basophilic stippling was not observed in this study. Anisocytosis and polychromatophilia are always present in the blood of the new-born. Poikilocytosis is often present. The pear shaped cells are usually smaller and paler than the poikilocytes seen in severe anemias.

20. The platelets are often larger in the new-born blood than in that of the normal adult. Their variations in size are greater than those ordinarily seen in the adult.

21. The neutrophil and eosinophil granulation is similar to that seen in adult blood. The azure granules tend to be less numerous, but when present, their size, distribution, and staining reaction are the same as in the average blood smear of a normal adult.

22. In five cases of marked icterus neonatorum no changes from the normal were noted in the total cell counts or in the differential counts.

23. The standard deviation and the coefficient of variability were determined for the absolute and relative counts of all types of blood corpuscles. The findings may be summarized as follows: (*a*) The red

blood cell count was the least variable of any of the cell counts, and its coefficient of variability averaged about 11 per cent. It stands midway between the variability in height and the variability in weight of the child at birth; (*b*) the variability of the blood platelets is very great at all times and averages over four times that of the red blood cells; (*c*) the coefficient of variability of the leukocytes is about from 20 to 25 per cent., or about one-half that of the platelets and twice that of the red blood cells; (*d*) the coefficient of variability of the total polymorphonuclear leukocyte count averages about 35 per cent., being about one half more than that of the total leukocyte count; (*e*) the coefficient of variability of the total lymphocyte count is about the same as that of the polymorphonuclear. It tends to decrease during the period of observation; (*f*) the variability of the cells having lesser total counts is very great, the coefficient of variability ranging from 85 to 200 per cent. In most instances the variability becomes less after the first day; (*g*) the nucleated red corpuscles are also very variable. The coefficient of variability reaches its maximum at about 215 per cent. on the second day; (*h*) the percentage counts of the various types of cells are, as a rule, more constant than the absolute counts; (*i*) the percentages of the commoner varieties of circulating blood cells, the lymphocytes and the polymorphonuclear leukocytes, show a coefficient of variability of from 20 to 25 per cent. The remaining varieties have a coefficient of variability of from 50 to 80 per cent., except for the basophils which have a variability of 100 to over 200 per cent.

24. The changes observed in the red blood cell, platelet and leukocyte count cannot be accounted for on the basis of blood concentration. The differential study emphasizes the fact that the variations noted in the new-born period are due to increased activity of the hemopoietic organs.

The evidences for increased neutrophil production are: (*a*) The polymorphonuclear leukocytosis, (*b*) the large numbers of metamyelocytes, (*c*) the presence of neutrophilic myelocytes, (*d*) the occurrence of unclassified promyelocyte types, (*e*) the increased vulnerability of neutrophils, (*f*) the very small P. M. N. neutrophils, (*g*) the occurrence of cells in which the cytoplasm is basophilic and the nucleus polymorphous.

The facts indicative of increased lymphocyte production are: (*a*) Early types of lymphocytes, (*b*) the presence of cells undergoing amitotic division, (*c*) the presence of Rieder cells, (*d*) the presence of plasma cells, (*e*) atypically large lymphocytes, (*f*) the increased vulnerability of the lymphocytes. (*g*) the occurrence of occasional Türke's irritation cells. Evidences in support of the concept of increased red cell production are: (*a*) polychromatophilia, (*b*) anisocytosis is always present, (*c*) poikilocytosis is occasionally seen, (*d*) nucleated reds are found in every new-born infant's blood, (*c*) megaloblasts are frequently observed, (*f*) naked red cell nuclei are often seen, (*g*) mitotic figures are present in instances of markedly increased numbers of nucleated red blood cells.

I wish to acknowledge my indebtedness to Dr. Scammon, under whose direct supervision this work was done. Without his valuable suggestions in all the phases of the problem, especially in the section on statistics, this study could not have been accomplished. I also wish to thank Dr. Hal Downey for his kind assistance in the hematologic section, and Miss Pearl Shalit for her services.

Abstracts from Current Literature

Anatomy and Physiology

THE VALUE OF THE HEMOGRAM IN INFANCY. CURT and STECHER FRANKENSTEIN, Ztschr. f. Kinderh. **37**:145, 1924.

The hemogram, or differential cell count of premature infants, shows the definite shifting to the left of Arneth. Many immature polymorphonuclear leukocytes are found there. The hemogram of full term new-born infants is also easily distinguished from that of adults. This differential cell count is of great value in the diagnosis and prognosis of disease in infants, especially in the acute infections, atrophy, and intestinal disturbances.

PETERMAN, Rochester, Minn.

INNERVATION OF THE VENO-CONSTRICTOR MECHANISM OF THE LIVER. HANS MAUTNER, Monatschr. f. Kinderh. **27**:385, 1924.

The conclusions are based on the following technic. A clamp was placed on the pulmonary artery causing a back-flow of blood into the liver, and then different drugs were investigated as to whether their effect increased or decreased the size of the liver's swelling.

In this way, Mautner concludes that the influence of the vagus, as well as split protein products, peptone, histamin and water tend to cause constriction.

On the other hand, stimulation of the sympathetic, as well as diuretics and hypertonic solutions, cause dilation.

GERSTLEY, Chicago.

Pathology, Bacteriology and Biochemistry

A BIOLOGIC STUDY OF ACIDURIC BACTERIA. PAUL R. CANNON (University of Mississippi), J. Infect. Dis. **34**:*227* (March) 1922.

A biologic study of sixty-four strains of *B. acidophilus* and thirty-four of *B. acidophil-aërogenes* was made. These organisms were isolated from ninety-three different sources, mostly from the sputum and feces of normal human adults. Dried autolyzed yeast was used as the basis for all the fermentation tests, and was particularly satisfactory for the study of these members of the aciduric group.

These bacteria are facultative anaërobes, but will grow well under aërobic conditions. They do not liquefy gelatin, and may or may not clot milk. They grow best in a reaction of p_H from 6 to 7, but will develop within the range of p_H 5.0 to 7.6 at least. When grown in dextrose yeast broth in mixed culture with *B. coli*, with an initial reaction of p_H 7.0 to 7.6, *B. coli* at first gains the ascendency, but *B. acidophilus* becomes predominant as the p_H approaches 5.

In the case of twenty-two strains, both aciduric and fermentative characteristics were practically constant for twelve months. The fermentation reactions for twenty carbohydrates were determined, all negative tests being checked at least twice.

A classification according to the scheme of Rahe is given.

. KENNEDY, Rochester, Minn.

CLINICAL AND EXPERIMENTAL EVIDENCE OF THE VIABILITY OF TRANSFUSED FOREIGN ERYTHROCYTES. HANS OPITZ, Monatschr. f. Kinderh. **27**:376, 1924.

The question to be answered was whether the benefits derived from blood transfusions were due to the foreign red cells themselves, or to the stimulus of the foreign blood on the child's bloodmaking organs. To solve this, Opitz injected separately both plasma and washed erythrocytes into an anemic child. He also injected whole blood and hemolyzed blood into a number of animals. By blood counts and blood chemistry he came to the conclusion that the good results are from the injected red cells themselves and that these remain viable for considerable time.

Gerstley, Chicago.

The Relation of the Substance Resisting Saponification to Rickets. H. Beumer, Ztschr. f. Kinderh. **37**:105, 1924.

Experimental evidence is cited, in support of the theory that the antirachitic substance in cod liver oil is found in that portion which cannot be saponified.

Peterman, Rochester, Minn.

Nutritional Disturbances

Do Height and Weight Tables Identify Undernourished Children? Louis I. Dublin and John C. Gebhart. Statement by Louis C. Schroeder. New York Association for Improving Conditions of the Poor, New York, 1924.

This timely article brings out an important principle: namely, that the determination of normality in children does not rest on any set weight standards. The investigation was made among the Italians of New York City and consisted of examination and records of 1,878 boys and 2,169 girls. It was found by this examination that 77.2 per cent. of the boys and 67.1 per cent. of the girls who were actually undernourished would have been missed entirely if reliance had been placed solely on the standard of the 7 per cent. under weight. With the 10 per cent. standard 89.8 per cent. of the boys and 81.8 per cent. of the undernourished girls would have been lost. On the other hand, in the well nourished children 97.6 per cent. boys and 94.5 per cent. girls were found to agree with the standard weight tables.

The main part of the article is supplemented by a short statement by Dr. Schroeder, regarding the standards he used in choosing these children and in designating them as undernourished. This article only lays further emphasis on the fact, well known to the medical profession, that final decision regarding nutrition normality in children depends not on single standards such as weight but on complete physical examination which can only be conducted by a properly equipped physician.

Grulee, Chicago.

The Influence of Environment on the Nutrition of Growing Animals. Rudolf Degkwitz and fifteen assistants, Ztschr. f. Kinderh. **37**:27, 1924.

In an effort to determine the influence of light on cell metabolism of young, growing animals, Degkwitz and his assistants carried on a large series of feeding experiments on young dogs. Pairs of dogs were selected from the same litter; one dog of each pair was kept in natural light, the other in darkness. Various diets were fed:

Light

Protein		*Carbohydrate*	
Low value fat (Light dog)	L_1	Low value fat	L_3
Full value fat	L_2	High value fat	L_4

Dark

Protein		*Carbohydrate*	
Low value fat (Dark dog)	D_1	Low value fat	D_3
Full value fat	D_2	Full value fat	D_4

After five months the animals were killed and examined: Anatomic, pathologic, and chemical examinations were made. The two animals of each pair were compared and the various organs analyzed. High value fat, when fed in combination with a large amount of protein exerted the most favorable influence on the skeletal growth. Low value fats, such as cocoa butter, plus an excess amount of carbohydrates caused the least growth. Light absence produced a lowering of the metabolic rate and changes in the chemistry of the ash residue similar to those found in rachitis.

In the interpretation of the findings, the author considers the possibility of adaptation of the animals to darkness. He also mentions a number of important factors which must be considered in an interpretation of experiments of this kind. Apparent well-being and gain in weight are not reliable criteria of nutrition results. The entire body must be examined and the ash residue analyzed to make complete conclusions.

Pairs of healthy young dogs as nearly alike as possible were selected. Following the experiment, the dogs were clinically and pathologically (sections, histology) well. Every dog kept in darkness showed a greater increase in weight than his control. The amount of the total body weight increase was influenced by the quality of fat. The soft tissue growth was equally good whether high value fat was fed with high protein or high carbohydrate. Since a sufficient amount of vitamin was supplied, the variations in growth can be ascribed to the fat. In the dogs kept in darkness the ash residue showed a relative decrease in calcium, phosphorus, sodium and magnesium, while the potassium showed a relative or absolute increase. The absence of light did not cause rachitis but caused a predisposition to rachitis. The soft tissues and the bones showed a calcium and phosphorus decrease. Histologically, the bones could not be distinguished.

Peterman, Rochester, Minn.

The Influence of High Protein Concentration in Infant Feeding. Marianne Eckert, Ztschr. f. Kinderh. **37:**1, 1924.

Eight healthy infants, from 5 days to 6¾ months of age, were placed on a concentrated albumin feeding. The infants were fed Dubo (whole milk with 17 per cent. sugar) with an increased albumin content of from 30 to 40 per cent. The increase was held at 30 per cent. for twenty-four to sixty hours and then increased to 40 per cent. In one case the 40 per cent. increase was maintained for six days. Following the high protein diets there was noted, regularly, a loss of weight without symptoms of ill health. The food was well taken. The stool was often foul smelling and somewhat mucoid. Following this diet there was no increase in the cellular elements of the blood and there was no increase in the serum protein. There was no elevation of temperature in any case. Return to the former diet was followed by an increase in weight without temperature changes. Eckert (and Pirquet) cannot subscribe to the "dynamic protein fever" theory, if water is given freely. At least there was no increase in the temperature following a concentrated protein diet in the eight cases studied. However, only two protein preparations were used (albulactin and aleuronat). Protein concentrations higher than 20 per cent. are not well tolerated.

Peterman, Rochester, Minn.

The Pathology of Milk Injury, Part 2. Feeding, Stool, Characteristics and Bifidus-Flora. Reinhold Ruhle, Jahrb. f. Kinderh. **104:**39 (Jan.) 1924.

The pathogenesis of "milchnährschaden" is connected in some way with bacteriochemical processes in the large intestine and is related to the kind of food. The author's purpose is to determine the degree of dependence of the bifidus flora on different components of breast milk, and if possible to produce a physiologic bifidus flora by dietary changes on artificial feeding. He studied 3,000 stools of normal infants from 2 to 7 months of age, as regards consistency, color, reaction to litmus, odor, and gram-stains of stool for flora.

He found that replacement of fat in artificial feeding by breast milk fat and in breast feeding by butter fat, did not change the characteristics or flora of the stools. Addition of cereals to breast milk up to 3 or 4 per cent. had no influence on the stools; addition of calcium salts and sodium phosphate up to 1.5 per cent. gave more alkaline and brighter colored, firmer and less frequent stools with degenerative bifidus forms, and more *B. coli* and cocci. The addition of egg albumen did not affect stools, though cow's serum to 5 per cent. changed stools toward those of "milchnährschaden." *B. coli* predominated. Removal of casein and whey protein did not give a bifidus flora.

By one method, he was able to produce bifidus flora and stool characteristics on artificial feeding in some, though not in every case; i. e., by using the filtrate of skimmed milk predigested, with pepsin plus an equal amount of water and 5 per cent. lactose plus 6 per cent. butter plus 3 per cent. "Weizenmehl" (wheat flour). None of the known artificial foods have produced this result.

In this paper, the author is dealing only with normal infants, so no therapeutic results of this mixture are presented.

Sutherland, Chicago.

Experiments Concerning the Bacterial Invasion of the Intestinal Tract, and Its Influence Upon Food. Eugene Stransky, Monatschr. f. Kinderh. **27**:388, 1924.

Professor Moll has shown that rabbits fed on a onesided milk diet become hyperirritable to electricity and show signs of nutritional disturbance. Stransky kept a number of animals on this diet until he had affected their state of nutrition and then made smears and cultures from the mucosa of the stomach and various parts of the intestine. The sick rabbits showed *B. coli* in smear and culture, besides a variety of other organisms throughout all parts of the gastro-intestinal tract.

The control rabbits showed isolated colonies in the stomach and duodenum. The small intestine, as far as the lower ileum, was sterile, after which *B. coli* were found in large numbers.

The experiments repeated on dogs did not give identical results. At no time was any part of the intestine of these animals found sterile.

The experiments were repeated on rats. The findings were intermediate between those of the dog and of the rabbit, being more frequently, however, like the rabbit. Of interest was the observation that if vitamin was absent from the diet, bacterial growth was luxuriant throughout the whole intestinal tract.

Gerstley, Chicago.

Prenatal Conditions

The Value of the Roentgen Ray in the Diagnosis of Atypical Pregnancies, with Report of Two Cases of Anencephaly Diagnosed Before Birth. Davis Spangler, Am. J. Roentgenol. **11**:238 (March) 1924.

Aside from the diagnosis of pregnancy and its position the roentgenogram is of value in determining the degree of contracted pelves, spinal curvature, the diagnosis of multiple pregnancy and as a medicolegal factor. The author feels that a roentgenogram should be taken before a cesarean section operation is undertaken, and except in extreme emergency, before operative interference in eclampsia. This obviates the embarrassment of delivery by cesarean section of a monster, a dead fetus or an extremely small baby. The size can be fairly well determined and the modus operandi may be arrived at in doing version on a foot or transverse presentation.

Anencephaly, or craniorrhachischisis, is one of the most frequent of fetal monstrosities. Kirkness, in 1911, reported one in every 900 deliveries in a series of 11,521. Of the theories involved, the author mentions early hydrocephalus with secondary rupture and atrophy of cranial membranes, changes or toxins in the amniotic fluid and faulty implantation of the ovum due to changes in the endometrium. In the two cases reported the anencephaly was diagnosed by roentgen ray, which showed the lack of cranial bones, and the diagnosis was confirmed by the pathologist after delivery. The author regards the idea that the roentgen ray may be harmful to the fetus as fallacious.

STULIK, Chicago.

Acute Infections

BRONCHOPNEUMONIE DU NOURRISSON. JEAN MEYER, Thésè de Paris, 1923.

The first part of this thesis is taken up with a clinical résumé of the condition. The author then speaks of two specific conditions—the asphyxial and the septic-toxemic states—which he describes in detail. The former, as may be supposed, tends to cyanosis and is accompanied by rapid breathing; the temperature is variable but is usually quite high. The septic-toxemic state is characterized by diminution in weight, suppression of urine, the usual facies, loss of appetite and diarrhea. The child refuses the bottle, thirst seems to have disappeared, the skin is flaccid, subcutaneous injections of fluids are only slowly absorbed, the heart is very rapid and the liver is enlarged and hard. This period does not last more than two or three hours. Just before death the body is covered with sweat, the pulse becomes very weak, and respiration is slow.

The author has then undertaken to study first, the asphyxial state, and later the septic-toxemic. Asphyxia or "anoxemie" depends on the retention of oxygen in the arterial blood. The lowering of this tension is the essential factor, and is characterized clinically by cyanosis, and an excessive lowering means the irremediable failure of the vital processes. As to the cause of this condition one may, of course, regard it as due to the diffuse pulmonary lesion but it also may be due to a failure of the tissue tolerance for oxygen. In other words, the tissues may be unable to take up the oxygen because of the toxic condition.

In the toxic infections he has taken into consideration two syndromes, the anorexia and the variation of the weight curve. The weight curve is due to the water content of the body increased with edema and decreased with dehydration. Special study has been made of the condition of perspiration. This study was made in the following way: The basal perspiration was that of a child awake and calm, proportion of twenty-four hours. Due account was taken of the amount of urine, stool and carbon dioxid excreted. A calculation was made from the food and the excreta, the difference being regarded as the basal perspiration. Hourly weights were then taken. In the normal child the relation of basal perspiration to elimination daily was about from 40 to 50 per cent., while in bronchopneumonia it was about 80 per cent. This runs parallel to the dehydration. In some, however, the perspiration was abnormally low caused by retention of the water.

He also examined the caloric loss in infants and found in the normal cases it amounted to from 60 to 70 per cent. In bronchopneumonia it is sometimes increased and sometimes diminished, but the intake of the food is always reduced and the relative size of the caloric loss is considerably increased. In normal infants half of the heat eliminated is by perspiration and the other half by radiation. In bronchopneumonia perspiration eliminates about 90 per cent. and the rôle of radiation is diminished.

One of the chief factors, therefore, in equilibration of tissue exchanges, caloric equilibrium and thermal regulation is perspiration.

The last of the treatise is taken up with a short chapter on prognosis, which contains nothing new, and on treatment. He strongly advises fresh air and sunlight, to prevent the child from chilling, and also change of position to prevent hypostatic pneumonia. The diet should be as abundant as possible. Warm baths are advised. He advises also serotherapy, not for its specific but for its general tonic effect. This necessitates large doses. For asphyxial syndrome oxygen is of value. Stimulation is likewise mentioned.

GRULEE, Chicago.

Bone Dystrophies of Variola. J. W. Cathcart, Am. J. Roentgenol. **11:**229 (March) 1924.

The author cites the work of Chiari, who reported nonsuppurative, sterile necrotic foci in the bone marrow in twenty-two necropsies on variola cases of different stages. Mallory found these foci in fourteen patients dying of variola and notes that they were more numerous in the short bones. Patients of the first age period who have variola may have these necrotic areas so situated as to involve the ossific centers and so alter the future development of the bone. The epiphyses may become altered and ankylosis, fusion and exostosis are frequently resultant. As a rule the greater deformity is found where the variola infection occurs in the first years of life.

Musgrave and Sisson reported deformities of the forearms and hands caused by variola contracted early in life. All of their twenty cases were native Filipinos.

A girl, American, aged 6 years, living in Mexico contracted severe variola three years ago, and during three months in bed the severe pains in the arms and legs simulated rheumatism. She gradually developed deformities of the forearms and wrists. The roentgenogram shows that the left ulna extended 2 cm. beyond the radius and deflected the hand to the radial side. There was a suggestive old necrosis of the lower end of diaphysis, and in the thickened radius the distal epiphyseal line was obliterated. In the right forearm the radial epiphysis of the elbow and the distal epiphysis of both ulna and radius were obliterated and the radial shaft was bowed out. There were old necrotic areas in the tibia and fibula of the left leg. The right clavicle was 2 cm. shorter than the left.

In the discussion, Phemister, before seeing the work of Musgrave, was inclined to consider the condition one of osteomyelitis of the metaphyseal regions due to pyogenic organisms entering through the skin.

Stulik, Chicago.

Specific Streptococcus Agglutinins in Concentrated Scarlatinal Serum. R. D. Herrold and Ruth Tunnicliff, J. Infect. Dis. **34:**209 (March) 1924.

Concentration with ammonium sulphate is useful for demonstrating specific streptococcus agglutinins in scarlatinal serum. Unconcentrated scarlet fever serum 1:10 fails to agglutinate hemolytic streptococci, specific for sarlet fever. When concentrated with ammonium sulphate, 25 per cent. of the scarlet fever serums collected before the eleventh day of the disease, and 92 per cent. of the serums collected after the eighteenth day, agglutinated scarlatinal strains of streptococci, but not the other streptococci tested. Serum, unconcentrated, and concentrated from diphtheria patients and from a patient who had scarlet fever two years previously, failed to agglutinate any of the streptococci examined.

Kennedy, Rochester, Minn.

The Influence of Scarlatina and Diphtheria on the Heart. A. F, Hecht, Ztschr. f. Kinderh. **37:**5, 1924.

Nine cases of cardiopathy which had developed during diphtheria were examined sixteen years after the onset of the infection. Seven per cent. of the patients had residual cardiac lesions, for the most part myocardial weakness. Six cases had developed cardiac complications during scarlatina nine and a half to twelve and a half years previously. Two patients had residual mitral lesions. The cardiac complications which develop during scarlatina offer a much better prognosis than those developing in diphtheria.

Peterman, Rochester, Minn.

Agglutinins for Pfeiffer Bacillus in Serum of Influenza and Measles Patients. W. B. Sharp and E. O. Jordan, J. Infect. Dis. **34**:305 (March) 1924.

Sharp and Jordan studied the serums of twenty-nine influenza patients, twenty-nine measles patients and twenty-seven other persons in regard to their power to agglutinate the Pfeiffer bacillus. They found that the serum of influenza patients agglutinates Pfeiffer bacilli to a greater degree and in a larger number of cases than does the serum of healthy persons.

Serum of measles patients does likewise, so that the presence of agglutinins for the Pfeiffer bacilli in influenza serum cannot be taken as evidence of any causal relation between the organism and influenza. There is no evidence that the observed increase in agglutinative power in measles serum is dependent in any degree on a secondary invasion by the Pfeiffer bacilli. The most plausible explanation seems to be that infections of various kinds increase the nonspecific or normal agglutinins of the blood, and that such relatively slight agglutination enhancement as is observed falls in this category and not in that of specific causal relation.

Kennedy, Rochester, Minn.

Use of the Roentgen Ray in Pertussis. R. D. Leonard, Am. J. Roentgenol. **11**:264 (March) 1924.

In collaboration with the staff of the Floating Hospital, 450 cases of clinical pertussis were examined and treated. The entire chest and lower neck alternating front and back were treated with a 5 ma. dose with a 6 inch spark back-up for four minutes, at a focus skin distance of 14 inches using a 1 mm. aluminum filter. This small dosage was used to prevent harm to the skin, thyroid or thymus.

Under the direction of Mallory not a single positive culture of the Bordet bacillus was obtained from nose, pharynx, larynx, trachea or turbinate curetting. In the one fatal case Mallory demonstrated the Bordet bacillus within the tissue of the trachea. This may be due to the fact that most of the cases were seen at the height of the paroxysmal stage and not at the early catarrhal stage.

Each child was given four treatments, unless marked improvement followed the second or third treatment. The treatments were given two days apart.

The bronchial glandular enlargement observed was much greater than that noticed in chests of children with measles, scarlet fever or diphtheria. It is the author's theory that the direct action of the roentgen ray on the bronchial lymph nodes produces the relief of symptoms.

There was a diminution in the severity of the paroxysms, and frequently a marked diminution in the number and vomiting was promptly relieved.

Compared to 200 cases untreated with roentgen-ray therapy, the course of the disease was definitely shorter only in the children from 1 to 2 years of age in the treated group. Exact comparison cannot be made, because many of the children treated with roentgen ray were also getting medication including vaccine.

In the discussion, Dr. Dunham regards the benefit due to aid in resolution of the simultaneous pneumonic condition, and Dr. Leonard states that there is some general effect besides local effect on the glands. The problem is to arrange for these children in a separate institution or in a roentgen-ray whooping cough clinic.

Stulik, Chicago.

Chronic Infections

The Influence of Pertussis on Tuberculosis. Ernst and Fuerst Koenigsberger, Ztschr. f. Kinderh. **37**:159, 1924.

In thirteen tuberculous children under 2 years of age, who developed pertussis, tuberculosis became active in nine. Sixty-one tuberculous children, from 2 to 14 years of age, developed pertussis; in six the tuberculosis became active. Of two hundred forty-six children with tuberculosis only fourteen cases had been preceded by measles, and four by pertussis. The tendency to exacerbation of a tuberculosis is much greater following measles than it is following pertussis.

Peterman, Rochester, Minn.

Quantitative Studies in Syphilis from a Clinical and Biological Point of View. No. X, Arsenic in Human Milk After Intravenous Injection of Salvarsan. J. A. Fordyce, Isadore Rosen and C. N. Myers, Am. J. Syphilis **8**:65 (Jan.) 1924.

Arsenic was not present in any considerable quantity in the milk of fifteen control cases under hospital conditions. Seventy-five specimens of milk from twelve mothers receiving active antisyphilitic treatment, were examined. After 0.6 gm. neo-arsphenamin, the average excretion in the milk expressed in milligrams of metallic arsenic per one hundred grams of dried specimen was: The first day, 1.25; second, 1.16; third, 0.70; fourth, 0.98; fifth, 1.31. The arsenic excreted in five days would be equivalent to about 0.03 gm. of neo-arsphenamin. The presence of arsenic in mother's milk is more constant than in either the blood or urine, and was found in appreciable amounts in one case four months after the last arsphenamin injection. A nursling, therefore, receives sufficient arsenic in the breast milk to be of "some therapeutic value." There should be energetic treatment of the mother during lactation, in addition to other forms of treatment of the infant.

Sutherland, Chicago.

Internal Diseases

Acute Aleucocytemic Leukemia in Childhood. H. Baer, Jahrb. f. Kinderh. **104**:1, 1924.

This is a detailed description and discussion of three fatal cases from 7 months to 7 years of age, having a hemoglobin of from 14 to 22 per cent., a color index of 1 + and a white count of 2,000 to 6,000. The symptoms covered a period of from one to two months before admission. There was extreme weakness, pallor and loss of appetite, slight fever and a tendency to hemorrhages especially into the gums. The spleen and liver were enlarged. These cases were considered leukemic on account of the predominance in the blood smears of lymphocytes and lymphocyte-like cells, (87 per cent.) and the small number of polymorphonuclear leukocytes (8.5 per cent.). There was also a diffuse lymphocytic infiltration of the lymph glands and the interlobar connection tissue of the liver. Two of these cases were of the myeloid type, and one a mixed myeloid and lymphatic. The etiology is unknown.

The blood picture of these acute leukemias is similar in several respects to that of aplastic anemia, but the course is more acute and the bone marrow is richer in cells with more nucleated red cells. The author considers acute leukemia to be much more common than aplastic anemia in children.

Sutherland, Chicago.

Adrenal. Erwin Thomas, Monatschr. f. Kinderh. **27**:343, 1924.

Thomas brings the literature of the adrenal up to date. The main evidence of the function of the gland as exhibited by cases of hypertrophy, is that it seems to be a factor leading toward masculinization, women with such tumors seeming to take on somewhat masculine qualities.

The gland seems perhaps to be part of a protective mechanism against poisons, as hemorrhages in the medulla are found in some cases of poisoning, and marked changes in the gland in fatal cases of scarlet fever and streptococcus septicemia.

The gland in its composition contains neutral fat and fatty acids, cholesterin and its esters and lipoids. Of these, the cholesterin especially, is stored, particularly in herbivora. It is questionable whether this process occurs in carnivora.

Of course the secretion of the medulla, the blood pressure raising element known as adrenalin, has long been described. Besides this, the gland may possibly have some concern with the metabolism of vitamins.

As regards its diseases, Addison's disease is very rare in children. Hemorrhage into the gland is not so very uncommon and is fatal in twenty-four hours.

Of interest is the observation that the adrenal is especially large in the new-born.

GERSTLEY, Chicago.

THYMUS GLAND. W. BIRK, Monatschr. f. Kinderh. **27:**321, 1924.

The usual methods of studying glandular function are rather difficult in the case of the thymus. Congenital absence is extremely rare without changes in other organs which might confuse the picture of pure absence of the thymus. Hypoplasia of the thymus might readily be confounded with normal involution, Furthermore, results of surgical removal are most uncertain. The conclusions of observers are utterly conflicting, and the findings ascribed by some investigators to removal of the thymus were probably due to poor hygiene of the kennels in which the animals were kept.

Studies by implanting grafts of thymus are more satisfactory than those concerning themselves with its absence. In certain animals, implanting thymus into the muscles leads to increased growth of that animal.

When all is said and done, our knowledge of thymus is based to a considerable extent on clinical observation. The association of sudden death with enlarged thymus has long been noted. Paltauf was one of the first to emphasize this association, but thought it was merely a coincidental finding, the main factor being a cardiac weakness. Escherich somewhat amplified this view by laying increased significance to the so-called "thymic constitution," believing the depression of the heart to be caused by an excessive thymic secretion.

These ideas have been challenged by a number of observations. Some cases of sudden death have been traced to myocarditis from other causes. Some cases have been found associated with hypoplasia of the chromaffin apparatus. Richter's idea is well known; namely, that the thymus is found to be large in practically all cases of sudden death, but that this is a normal finding, for, in cases of disease, the thymus atrophies so quickly that on necropsy it is found to be abnormally small. Lastly, the idea of hypersecretion has been attacked by the observation that the sudden death has been due to suffocation caused by the pressure of the enlarged organ.

Birk still believes, however, that a very small group of cases of sudden death may be explained on a hypersecretion basis. His reasoning is clinical. First, a certain number of patients with Basedow's disease die suddenly on the operating table. Necropsy reveals an enlarged thymus. Hence the reasoning that excessive thymic secretion might be a cause. Another argument of Birk's is the lymphocytosis found in status lymphaticus is found in other conditions associated with thymus hyperplasia, such as myasthenia gravis. This might suggest an excessive thymus secretion.

Birk concludes his article by attempting to show that the thymus is related to the testis, ovary, adrenal, thyroid and parathyroid.

GERSTLEY, Chicago.

THYROID GLAND. E. SCHIFF, Monatschr. F. Kinderh. **27:**359, 1924.

It is interesting to note that aplasia of the thyroid gives no symptoms for some weeks after birth. In all probability the child is born with a supply. Schiff makes the statement that the fetal thyroid contains no iodin, but in the discussion following his paper this point was disputed.

As regards the functions of the thyroid, besides its effects on metabolism, it is undoubtedly concerned to some extent in the mechanism of growth, for all cretins are dwarfs.

In myxedema there is a popular tradition that the tolerance of the body for sugar is effected. This is not invariably true. There are perhaps vagotonic and sympathicotonic types of this disease which have their effects on sugar tolerance and muscle spasticity.

The child has a remarkable tolerance to thyroid and even through the school age, goodly doses of the extract while causing the same objective symptoms as the adult, do not seem to cause the child the same subjective sensations.

As regards the diseases, a true form of Basedow's disease is very rare in a child. The question of cretinism is not settled either. It is definitely related to the thyroid, but just how is uncertain.

In treatment, thyroid extract is of value in myxedema, but is not a cure. It seems to bring the patient to a certain stage and beyond that it does no further good.

GERSTLEY, Chicago.

CALORIMETRIC STUDIES ON INFANT CRETINS. FRITZ TALBOT, Ztschr. f. Kinderh. **37**:98, 1924.

The technic of the Talbot basal metabolism determination of infants is described in detail. The readings in two cases are given and the results of treatment enumerated in tables. Hypothyroidism presents a definite low basal metabolic rate during the first six months of life. These cases, according to Talbot, can be diagnosed only by obtaining the basal metabolic rate.

PETERMAN, Rochester, Minn.

THE CONSTITUTION AND REACTIONS OF THE NERVOUS CHILD. CARL POTOTZKY, Ztschr. f. Kinderh. **37**:24, 1924.

Zappert's classification of the neuroses of childhood, although more elaborate, suffers from the same defects as the more simple classification. Zappert divides the neuroses into: 1. Neuropathies. 2. Psychopathies. 3. Habit Neuroses. 4. Imitation neurosis. 5. Anxiety neuroses. 6. Compulsion neuroses. 7. Hysteria.

Pototzky's classification consists of: 1. Neuropathies. 2. Psychopathies. 3. Hysteria. Both classifications, he says, group together many unequal and dissimilar factors.

PETERMAN, Rochester, Minn.

THE PATHOGENESIS AND THERAPY OF TETANY. KURT SCHEER and ADOLF SALOMON, Jahrb. f. Kinderh. **104**:65 (Jan.) 1924.

The authors present further work on the mineral metabolism in spasmophilia as affected by hydrochloric acid milk, calcium chlorid and ammonium chlorid. Scheer had previously demonstrated that hydrochloric acid milk decreased the electrical and mechanical excitability. In this series, the calcium content of the blood serum, which is decreased in spasmophilia, was definitely increased toward normal under treatment with hydrochloric acid milk and by calcium chlorid.

The acid soluble phosphate was increased in tetany; the lipoid phosphorus varied being slightly increased in usual tetany cases, but distinctly decreased in the severe cases.

The calcium phosphorus quotient was decreased and this in inverse ratio to $\frac{\text{acid soluble phosphorus}}{\text{lipoid phosphorus}}$. With treatment, there was generally a rapid drop in acid soluble phosphorus, and in high phosphate tetany, an increase in lipoid phosphorus. The changes in calcium content were slower.

SUTHERLAND, Chicago.

Surgery and Orthopedics

The Surgical Treatment of Lateral Cervical Fistulae. Frederick Christopher, Surg. Gynec. & Obst. **38**:*329* (March) 1924.

The work of Wenglowski in 1912 brought out the fallacy of the branchiogenetic theory of the origin of lateral cervical fistulas. His ideas are based on a study of serial sections of seventy-eight embryos, 147 child cadavers and fifty-nine adult cadavers, besides a study of twenty-one cases of actual neck fistulas or cysts. His conclusions are as follows:

1. In man five or six branchial arches develop, and the same number of clefts or grooves. The grooves are not open.

2. The neck sinus—sinus cervicalis—is built by the approximation of the lateral borders of the neck, breast, and under border of the third arch and not the second as His contended.

3. In embryos as well as in adults the branchial apparatus does not lie from above downward but from front to back. Its inferior border and the inferior border of that part which arises from it are made by the line which passes through the inferior border of the hyoid bone.

4. In the beginning of the second month, the entire branchial apparatus as such disappears. It may leave behind it portions of many layered epithelium, or even particles of cartilage lying freely in the tissue. All the vestiges are usually found above and dorsal to the hyoid. The branchial apparatus cannot leave remnants in the neck below the hyoid.

5. The thymus originates from the third pharyngeal pouch, in the form of a long canal running obliquely from the lateral pharyngeal wall to the sternum, where the characteristic thymus substance begins to develop.

6. The thymic duct usually disappears either partly or completely. Occasionally, the entire duct or one of its parts may persist.

7. The vestiges of the thymic duct may change into a lateral cervical fistula or cyst. If the entire duct persists, a complete fistula results; when only a part of it, an incomplete one.

8. The anatomic situation of the lateral fistula corresponds very closely with the course of the thymic duct. The walls of the lateral fistulas are generally covered with squamous epithelium, but ciliated epithelium is occasionally found.

9. The lateral thyroid lobes also have a short canal which disappears early. By analogy with the thymic duct one can consider that this canal may also persist and form fistulas and cysts.

The author cites a case of a young girl on whom he operated for lateral cervical fistula by the von Hacker method. The tract was injected with methylene blue and dissected out completely, the upper end opening into the nasopharynx. The result was a complete cure.

Miller, Chicago.

Teleoroentgenography as an Aid in Orthopedic Measurements. P. M. Hickey, Am. J. Roentgenol. **11**:*232* (March) 1924.

By using a long cassette fitted with two sets of 14 by 17 intensifying screens accurately matched end to end, the author obtained a total film length of 34 inches and a width of 14 inches. With the tube at 7 feet, accurate measurements of the lower limbs were made. It was used to good advantage in measuring the femur and tibia in congenital dislocation of the hip, and in hypoplasia following anterior poliomyelitis and tuberculosis of the hip. Lewin, in the discussion, regards this method very useful in arriving at the amount of bone to be removed in leveling a pelvis of curvature of the spine, with inequality of length of legs.

Stulik, Chicago.

Book Review

Lehrbuch der Grenzgebiete der Medizin und Zahnheilkunde. With the collaboration of Prof. Dr. O. Buettner, Rostock i. M.; Prof. Dr. G. Finder, Berlin; Prof. Dr. E. Fuld, Berlin; Prof. Dr. F. Grossmann, Berlin; Prof. Dr. A. Gutmann, Berlin; Dr. E. Herzfeld, Berlin; Ministerialrat Dr. F. Koelsch, München, Geheim Sanitäts-Rat; Dr. H. Kron,* Berlin; Dr. R. Ledermann, Berlin; Dr. J. Misch, Berlin; Dr. H. Muchsam, Berlin; Dr. G. Tugendreich, Berlin. Editor, Dr. J. Misch. 2 Volumes. Third Edition, with 596 partly colored illustrations. Vol. 1, pp. 700. Vol. 2, pp. 682. Leipzig, F. C. W. Vogel, 1923.

By leaving a greater margin on the page, the remarks of the dentist editor, Dr. Misch, are easily recognizable because of his unusual acquaintance with many fields of medicine. This gives a certain uniformity of treatment. It is hardly possible to give more than an idea of the scope of the work. The headings of the main divisions are: "Mouth Digestion, Salivary Glands, Inflammations of Salivary Glands, Inflammations of Mucous Membrane of Mouth." "Disturbances of Development, Internal Secretion." Exogenous intoxications with such substances as are used in dental work. This division contains special chapters on narcotics and the theories of narcosis. "Diseases of Metabolism and Blood." "Infectious Diseases." "Circulatory Diseases." "Stomach Diseases in Their Relation to Diseases of Teeth and Mouth."

The pediatrician will be particularly interested in the chapters dealing with the diseases of children. "Anatomy and Physiology" of the suckling and of the secretions of mouth and saliva are discussed. "Dentition" is given its proper space, and perhaps a little too much significance is attached to its possible dangers. "The Relation of Diseases of Children to Diseases of Teeth and Mouth" includes rachitis, spasmophilic diathesis, tuberculosis, scrofulous and exudative diatheses, hereditary syphilis, scurvy, and acute osteomyelitis. "Acute Infectious Diseases" include chickenpox, measles, german measles, scarlet fever, and diphtheria. "Primary Disease of the Mouth," "Diseases of the Tongue," and "Malformation" form other subdivisions, while some pages are devoted to the care of the mouth in childhood, the sucking of the thumb and other bad habits, as well as to narcosis, general and local, in childhood. The importance of proper care of the milk teeth is strongly emphasized. It is truly remarkable how many dentists do not seem to understand this, not to mention the lack of knowledge on the part of physicians.

The next big subdivision deals with the nervous diseases subdivided into "Disease of Peripheral Nerves," "Organic Disease of Cord and Brain," "Mental Diseases," "Abnormal Condition with Nervous Symptoms," and "Hypnotism and Suggestion."

The fourth large subdivision is devoted to "Syphilitic Diseases," where the pathologic anatomy, subjective complaints and disturbances of function, diagnosis, transmissibility to animals and immunity, prognosis, heredity, prophylaxis of mouth syphilis, distribution and therapy are discussed. This concludes the first volume.

The second volume opens with the "Diseases of the Skin," including the occupational types. The division of "Diseases of Women," including obstetrics, contains many interesting data. In the seventh division, "Diseases of Nose, Throat and Larynx," the influence of mouth breathing on the mandibles and on occlusion of the teeth is treated at length. These chapters are of the greatest interest to the pediatrician. The eighth big subdivision covers "Diseases of the Ear." The ninth subdivision takes up "Diseases of the Eye," and the tenth deals with "Industrial Diseases." An index closes the second volume.

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* Dead.

At times it seems that the purely medical text could be shortened with advantage. The book is of great interest.

News and Comment

There will be as guests of the Pediatric Section at the A. M. A. Convention this year, Dr. Leonard Findlay of Glasgow University, Edinburgh, Scotland, and Professor Heinrich Finkelstein of Berlin. Dr. Findlay is well known for his recent work on "Rickets," and Dr. Finkelstein for his work on "Diseases of Nutrition" and also for a most excellent textbook on "Diseases of Infancy."

The American Pediatric Society will hold its thirty-sixth Annual Meeting on June 5, 6 and 7, at the Maplewood, Pittsfield, Mass. Dr. D. M. Cowie of Ann Arbor, Mich., will preside as President. The program will consist of six sessions with a total of twenty-six papers. This program gives a commendable admixture of both clinical and laboratory papers.

CORRECTION

In the article of Dr. D. C. Mebane, THE AMERICAN JOURNAL OF DISEASES OF CHILDREN, March, 1924, page 219, first paragraph, third line, the phrase "the prevention of mental disease" should read "the prevention of dental disease."

American Journal of Diseases of Children

Vol. 27 JUNE, 1924 No. 6

STUDIES IN GROWTH

I. GROWTH OF NORMAL CHILDREN *

FRITZ B. TALBOT, M.D.
BOSTON

The need for normal figures on the growth of different parts of the body presented itself to me as a result of my studies on the growth and metabolism in pathologic cases during the last two years.[1] Since these data were not available, figures were compiled from a series of body surface measurements, taken, according to the Du Bois linear formula, on a group of clinically normal American children on whom studies had previously been made to determine the normal standards of basal metabolism.[2] These were average children within the accepted normal limits of height and weight for age, and do not represent exceptionally well nourished or poorly developed children. A description of these children has been given in an earlier publication.[2]

The measurements were plotted on charts, and smoothed curves drawn to indicate the trend of growth of the different parts of the body. These curves do not represent mathematical averages. The distribution of the dots on either side of the curve show the normal deviation from the average, which must be taken into consideration in all instances.

In estimating growth the weight to age and height to age ratio are most commonly used. The height and weight curves of this series are presented in Charts 1 and 2. These measurements were taken without clothing.

The curves of growth in height and weight of this series show a close uniformity to the Crum-Wood curve, but are lower than the curves of private school children measured for Holt in New York [3] and Benedict and Talbot in Boston.[2] This is owing to the fact that this series represents a group of average children, while the private school group represents children living in exceptionally good surroundings.

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* Received for publication, March 24, 1924.

* From Children's Medical Department, Massachusetts General Hospital.

[1] Talbot, F. B.: Tr. Am. Ped. Soc. **35**:322, 1923.

[2] Benedict and Talbot: Carnegie Ins. Wash. Publication No. 302, 1921.

[3] Holt, L. E.: Standards for Growth and Nutrition, Am. J. Dis. Child. **16**: 359 (Dec.) 1918.

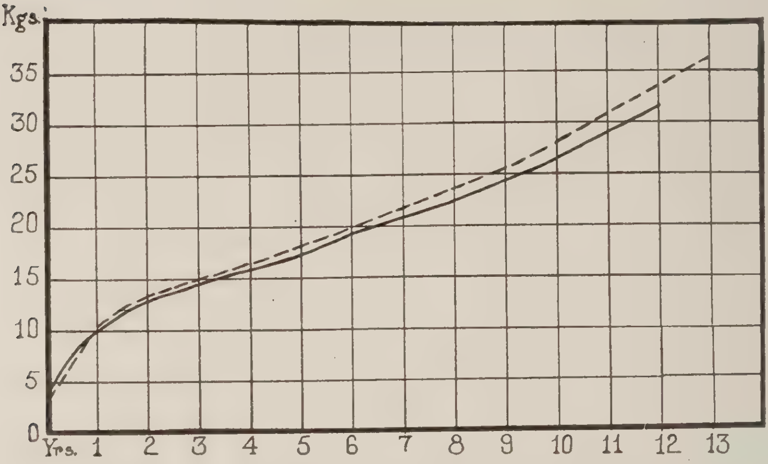

Chart 1.—Weight referred to age. In these charts, the broken line represents boys; the straight line, girls.[2]

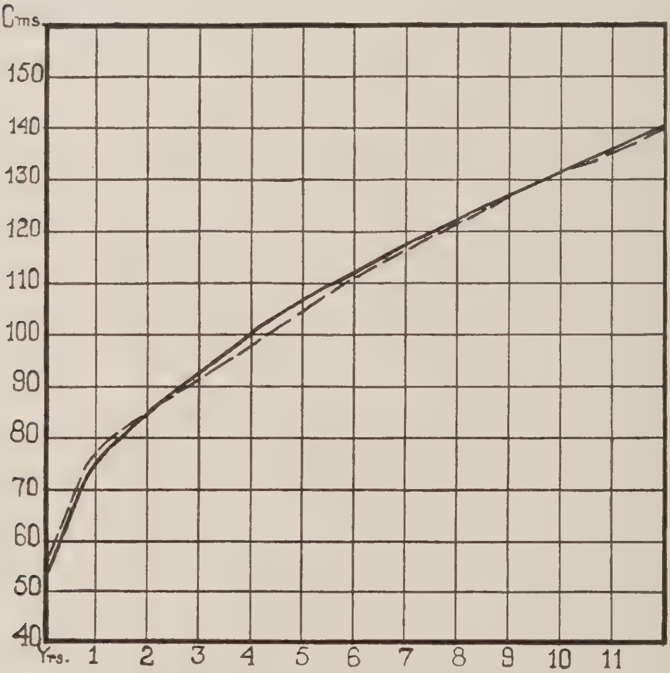

Chart 2.—Height referred to age.[2]

In order to obtain accurate data concerning relative body proportions; the children should be grouped according to weight for height which admits of less variability than age. Measurements of growth from the standpoint of stature are presented in Chart 3.

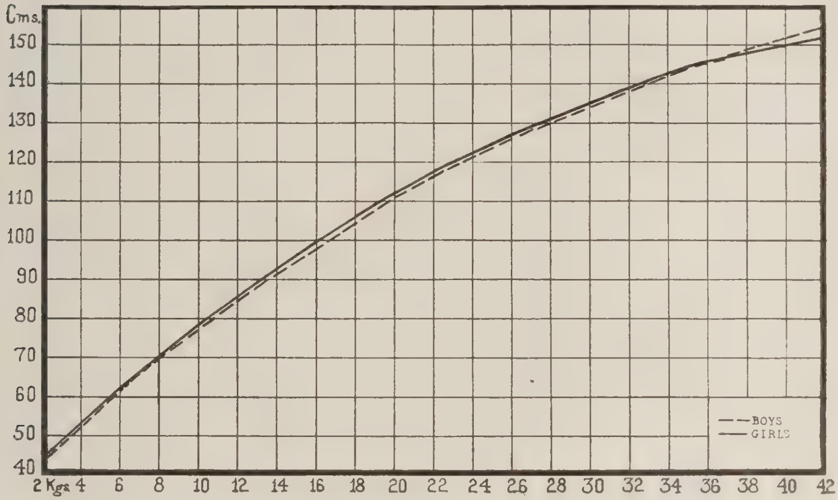

Chart 3.—Height referred to body weight.[2]

Circumference of Head.—The measurements of the development of body proportions are based on growth according to age. Charts 4 and 5 show the growth curve of the circumference of the head of boys and girls. This was measured from the occiput around the frontal bosses. Each dot represents the measurement of a child at a given age.

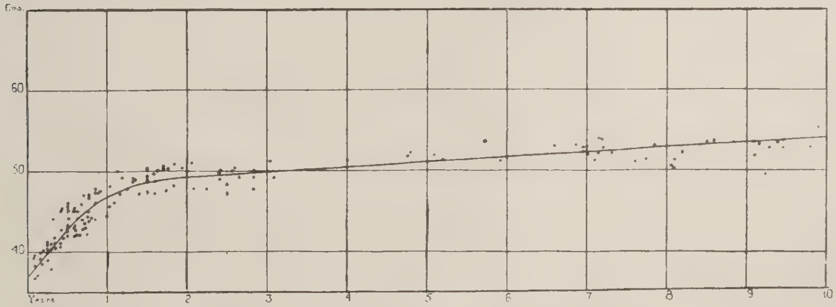

Chart 4.—The circumference of boys' heads.

The circumference of the head of boys is somewhat larger than that of girls. The very rapid increase in the size of the head during the first year of life in both sexes is followed by a gradual regular increase up to the age of 10 years. This great increase in the circumference of the head during the first year corresponds with the very rapid growth of the brain, which is said to double its weight during the first 8 months of life.[4]

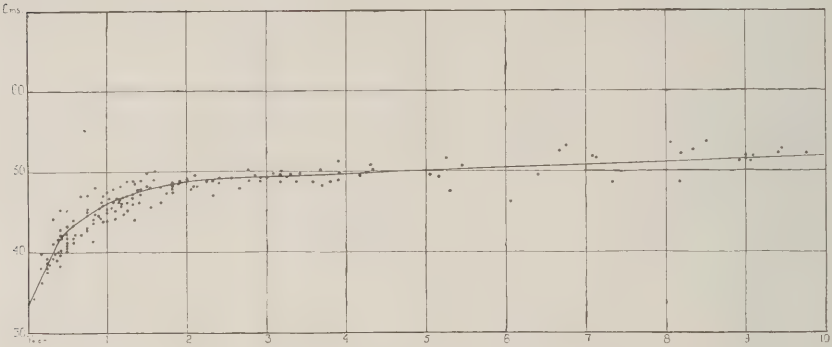

Chart 5.—The circumference of girls' heads.

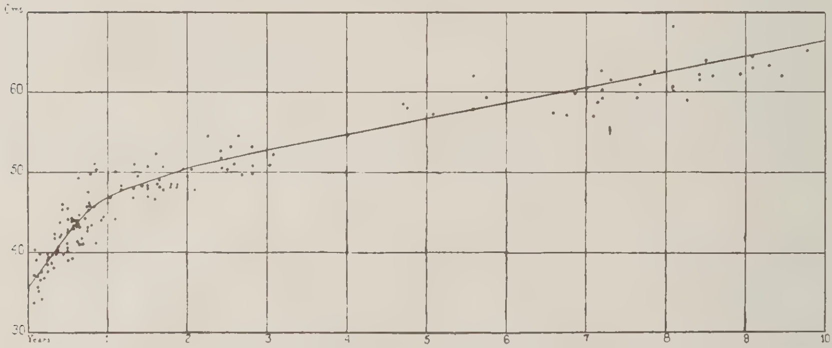

Chart 6.—Chest circumference, boys.

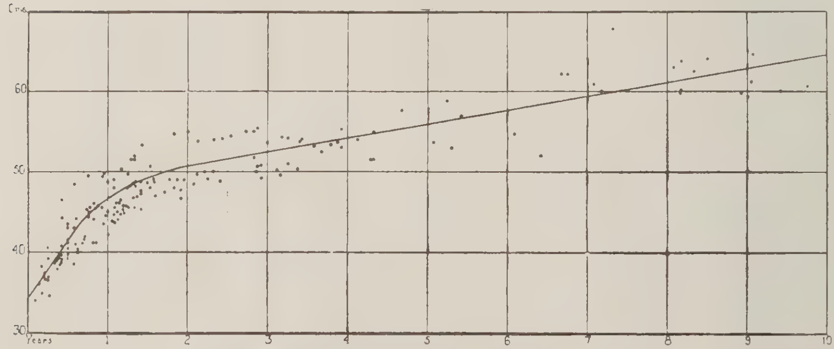

Chart 7.—Chest circumference, girls.

Circumference of Chest.—Measurements of the circumference of the chest (Charts 6 and 7), were taken over the nipples half way between full inspiration and expiration.

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4. Gundobin: Die Besonderheiten des Kindesalters, Berlin, 1912.

A close correlation is seen in the rate of growth of the chest in both sexes. The circumference of the head and chest is almost identical until 18 months of age, after which the circumference of the chest increases much more rapidly than that of the head.

Circumference of Abdomen.—Measurements of the circumference of the abdomen were taken over the umbilicus. There is a fairly close uniformity in the trend of the curve in both sexes. The great diversity in the distribution of the dots, especially in infancy, is explicable by the fact that a recent meal or gas may distend the abdomen and thus increase its circumference.

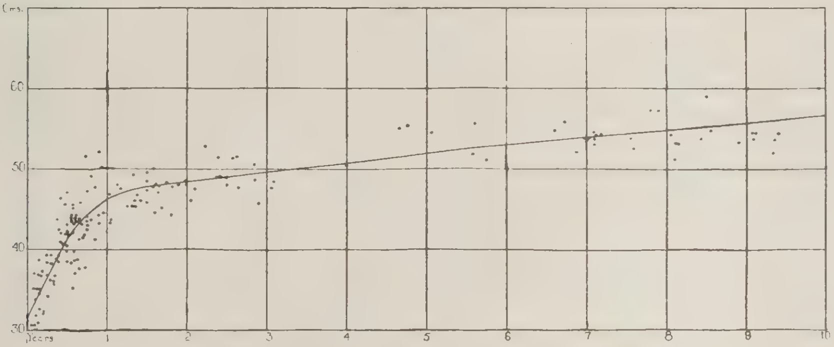

Chart 8.—Circumference of abdomen of boys.

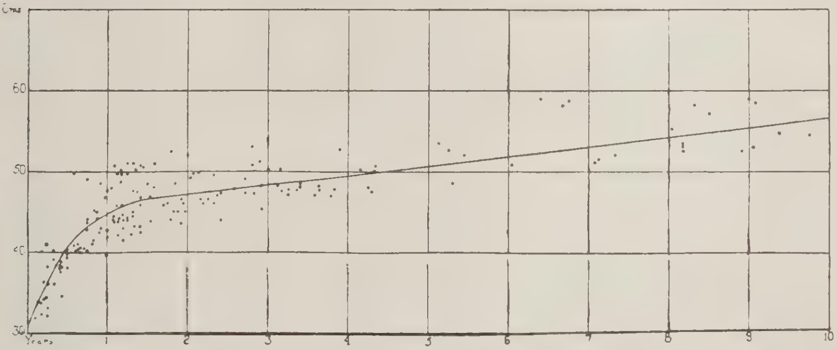

Chart 9.—Circumference of abdomen of girls.

Length of Trunk.—Measurements of the trunk were taken from the upper end of the sternum to the top of the pubis. Such measurements are very difficult to obtain in early infancy and should only be carried out with the infant lying flat on his back, on a smooth surface, in order to insure a perfectly straight spine and thus avoid errors due to flexion or extension.

These curves show a close uniformity in the rate of growth of the trunk in both sexes.

Length of Legs.—Leg measurements of the children are seen in Charts 12 and 13. These measurements were taken from the top of the pubis in the mid-line to the bottom of the foot.

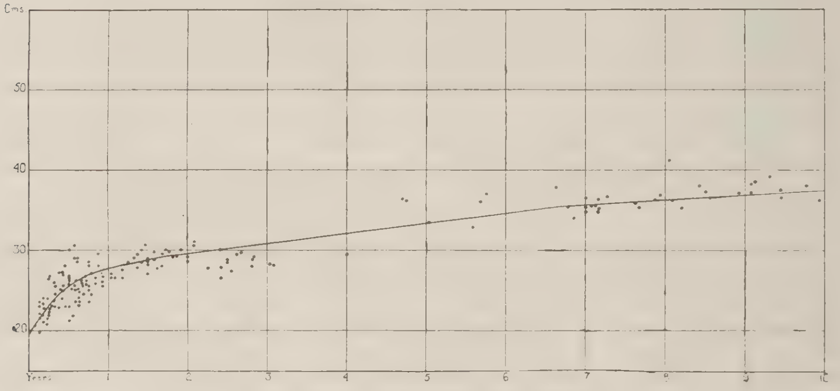

Chart 10.—Length of trunk, boys.

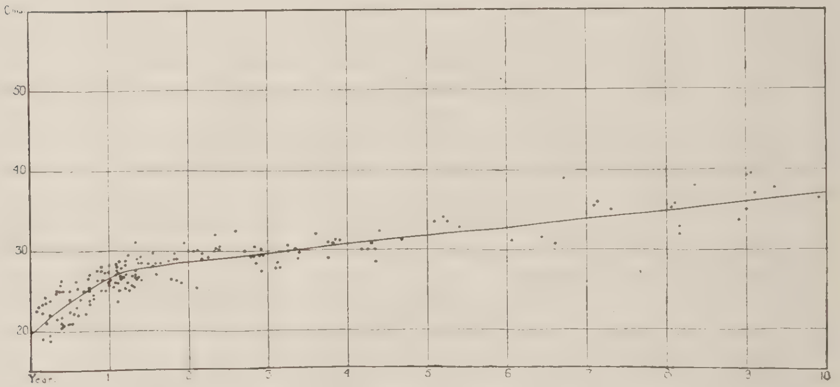

Chart 11.—Length of trunk, girls.

There is very little variation in the length of the leg of the two sexes up to the age of 6 years, at which time the rate of growth is greater in boys than in girls. The relatively greater growth of the legs than trunk is in conformity with the transition from the infantile proportions, in which the legs form three eighths of the total height, to that of the adult, in which they are about one-half of the total height.

Length of Foot.—Measurements of the length of the foot were taken from the heel to the tip of the great toe. There is very little if any difference in the length of the foot of boys or girls up to the age presented.

Total Length of Arm and Hand.—This was measured from the tip of the acromion process to the end of the second finger. Differences are more apparent in the length of the arm of boys and girls. From 2 to 6 years there is a greater length of arm in girls; from 6 years on it is greater in boys.

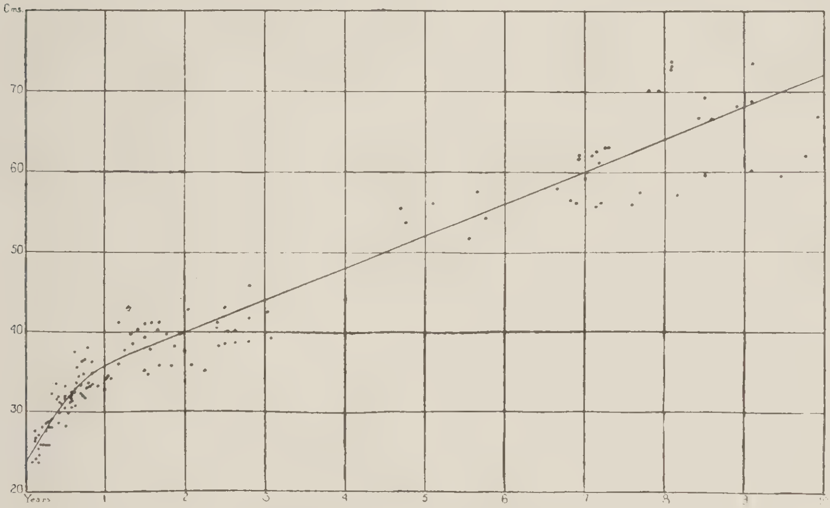

Chart 12.—Length of leg, boys.

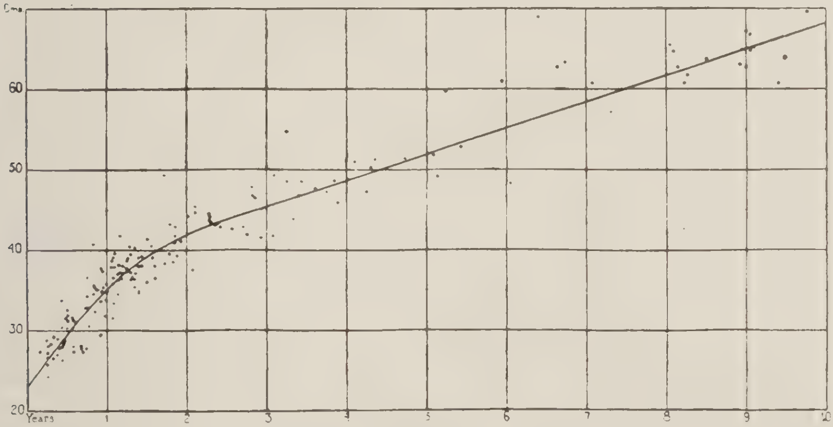

Chart 13.—Length of leg, girls.

COMMENT

These charts on the development of body proportions show very little sexual differentiation. A study of the curves leads to the conclusion that there is an "expected growth" for a normal individual. Measurements of normal children may either be applied to the curves at intervals and their relative physical development estimated, or comparison of single observations may be made in order to show their relation to the normal.

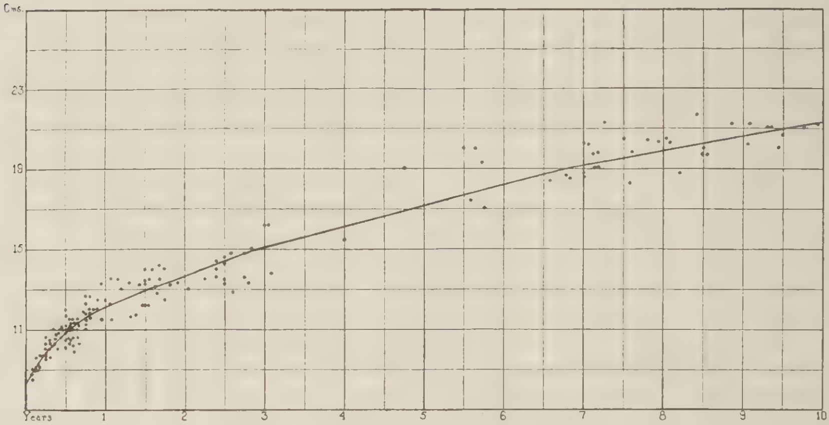

Chart 14.—Length of foot, boys.

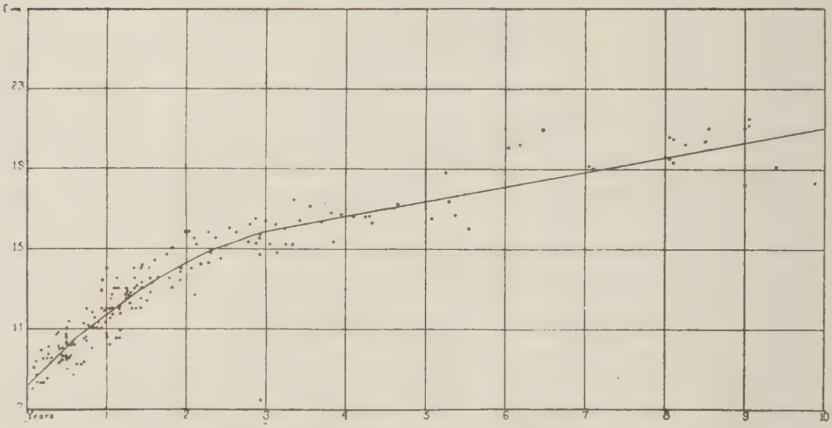

Chart 15.—Length of foot, girls.

Abnormal cases may be compared with these curves to determine in what respect their physical development differs from the normal. This has been done with cretins,[1] mongolian idiots and premature infants.[5]

The effect of treatment on the growth of abnormal children may also be studied by comparing them with these curves. If the growth curve runs parallel with or falls away from the normal curve, treatment has not affected growth. If, on the other hand, the growth curve approaches or reaches the normal curve, treatment may be said to have stimulated growth.

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[5] To be published.

The interpretation of results of basal metabolism studies in childhood is very difficult, principally because of the differences due to physical development; these differences becoming more marked as the child approaches puberty. It is, therefore, very important to estimate the physical development of a child whose basal metabolism is to be determined. This may be done by comparing the body measurements with the foregoing curves of growth of children of the same age.

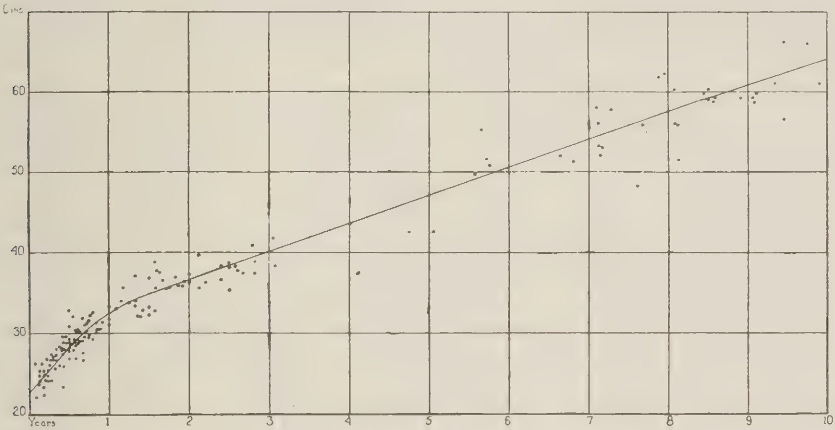

Chart 16.—Length of arms, boys.

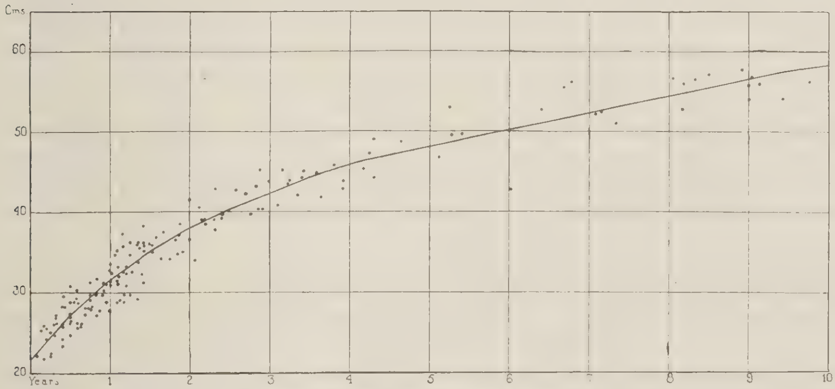

Chart 17.—Length of arms, girls.

If the development is found to be abnormal, the basal metabolism should then be compared with that of children of the same physical development irrespective of age. This is seen in cases of malnutrition and undernourishment which are accompanied by variations in the basal metabolism.[6]

SUMMARY

Growth curves of clinically normal American children are presented. They may be used as a means of comparison in the study of growth of untreated cretins, mongolian idiots and other abnormalities of growth, and are of value in determining the physical status of a child whose basal metabolism has been studied.

Body Measurements of Premature Babies

Case	Sex[*]	Age, Days	Wt., Kg.	Ht., Cm.	Sitting Ht., Cm.	Length				Circumference			Estimated Prematurity Days
						Trunk, Cm.	Arm, Cm.	Leg, Cm.	Foot, Cm.	Head, Cm.	Chest, Cm.	Abdomen, Cm.	
25	♀	1	0.727	34.5	23.3	12.8	14.4	14.2	4.9	23.1	20.3	16.9	—90[‡]
11	♂	18	0.992	....	....	15.9	16.9	14.9	6.03	27.6	15.2	20.3	—75
		38	1.191	38.0	....	13.3	16.1	16.2	6.1	28.0	26.0	19.7	—55
22	♀	7	1.304	38.0	25.0	12.5	17.2	14.3	6.0	25.2	24.0	24.0	....
1	♀	8	1.361	42.0	28.0	14.3	17.4	16.5	6.0	28.7	23.0	21.8	—60
19	♂	28	1.460	44.5	....	15.8	17.8	17.9	6.4	29.9	22.9	22.5	—30
3	♂	18	1.474	42.5	26.5	17.0	17.3	17.5	6.5	30.2	25.0	23.2	....
		34	1.843	42.5	29.1	15.1	17.7	18.1	7.0	31.2	25.0	24.0	....
13	♂	51	1.58	40.5	....	15.0	16.4	18.8	6.0	29.2	28.3	25.0	— 9
2	♂	18	1.644	46.0	28.0	15.0	19.8	18.3	6.7	31.0	27.5	26.5	....
		34	2.155	47.0	30.5	15.7	20.3	18.0	7.2	31.9	27.7	30.1	....
7	♀	21	1.687	47.0	29.5	14.2	16.4	16.4	6.0	30.0	25.0	21.0	—30
		65	2.467	47.1	35.4	19.1	17.9	19.9	7.0	35.2	26.2	26.5	+ 5
9	♀	3	1.701	43.5	28.5	13.0	17.9	17.6	6.5	31.5	24.8	22.8	....
		24	1.900	45.5	29.1	15.1	18.1	19.0	7.1	31.5	27.2	25.4	....
8	♀	23	1.723	45.0	30.5	17.3	18.3	18.7	6.1	29.5	26.8	29.0	—37
5	♀	12	1.744	43.0	27.4	15.1	18.9	18.7	6.6	29.3	25.5	23.0	....
		25	1.970	46.8	29.2	14.5	17.6	18.0	7.2	30.0	26.0	23.3	....
10	♂	7	1.744	43.0	26.2	14.9	16.4	16.3	6.6	29.8	24.5	24.0	—44
4	♂	12	1.76	42.5	....	14.0	19.0	17.9	6.7	30.0	25.0	23.0	....
		24	1.829	45.5	28.5	14.0	19.0	18.9	7.0	30.5	27.8	28.0	....
6	♀	14	1.772	43.8	29.0	16.2	15.5	17.5	6.1	29.7	26.7	25.3	—39
		68	2.86	47.0	....	16.1	16.0	19.1	7.3	33.4	31.1	30.6	+19
		97	3.02	53.0	34.0	19.5	20.5	20.4	7.6	34.5	33.0	33.7	+46
		14 mo.	6.861	68.7	47.2	24.1	28.6	29.9	10.8	44.3	41.2	40.0	....
		17 mo.	7.825	69.8	48.2	26.6	30.4	32.4	10.4	43.7	43.8	43.5	....
18	♂	21 da.	1.895	46.1	....	16.9	18.0	17.5	7.2	32.2	25.7	26.0	....
17	♂	28 da.	1.999	45.8	....	18.8	18.8	18.4	6.2	31.9	26.2	25.3	—60
23	♀	16 da.	2.098	46.5	....	16.2	19.6	20.3	7.8	30.6	36.1	24.4	....
15	♀	45 da.	2.155	45.5	....	19.0	18.1	19.1	7.0	32.3	28.9	27.5	....
16	♀	45 da.	2.339	47.7	....	21.0	17.7	21.0	7.1	32.4	29.0	27.8	....
24	♂	16 mo.	10.9	81.0	....	26.7	30.2	35.0	11.5	49.0	50.0	53.0	....

[*] In this column, ♀ indicates female; ♂, male.

[‡] Measurements taken at necropsy.

II. GROWTH OF PREMATURE INFANTS

The curves showing the growth of normal children have been presented. These curves were constructed from measurements taken according to the Du Bois linear formula.[7] The following measurements of a series of premature infants, on many of whom basal metabolism studies have already been reported,[8] were taken in the same manner and are presented in the accompanying charts for comparison with the growth curves of the normal series.

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[6] Talbot, F. B.: Severe Infantile Malnutrition, Am. J. Dis. Child. **22**:358 (Oct.) 1921.

[7] DuBois, Delafield, and DuBois, E. F.: The Measurement of the Surface Area of Man, Arch. Int. Med. **15**:868 (May) 1915.

Individual measurements of these premature infants are presented in the table.

The measurements of these premature infants, of varying ages post-partum, are shown in the following charts in relation to the normal curve. Since it was difficult to estimate accurately the amount of prematurity, they are compared with infants of the same age after birth.

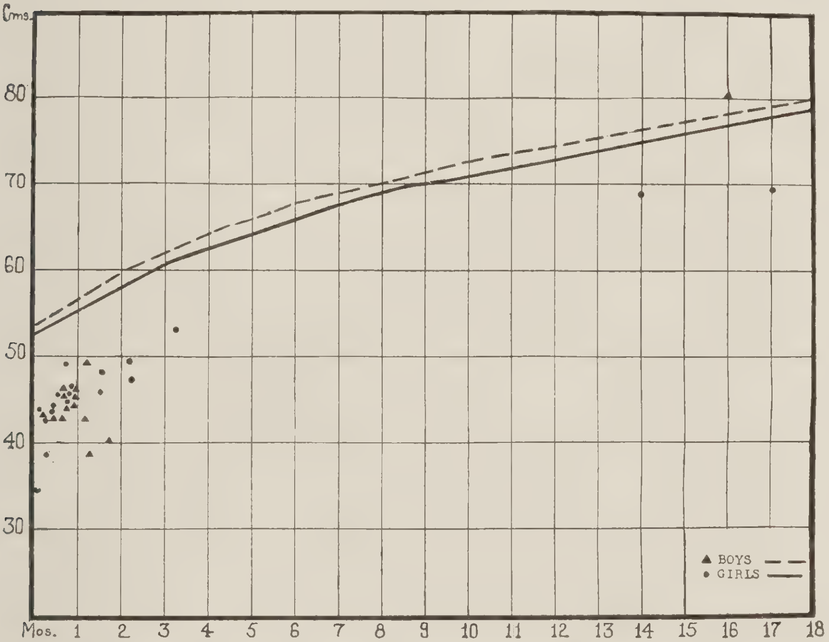

Chart 18.—Height referred to age in premature infants.

If it had been possible to measure the exact degree of prematurity, it would have been instructive to compare their development with the fetus of the same age.

Chart 19 shows that there is approximately the same relationship between the height and weight of premature and normal infants. The projection of the curve of normal children to the left would approximately bisect the dots of the premature infants.

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[8] Talbot, F. B., and Sisson, W. R.: Proc. Soc. Exper. Biol. & Med. **19:** 309, 1922; Talbot, et al.: The Basal Metabolism of Prematurity, Am. J. Dis. Child. **24:**95 (Aug.) 1922; The Basal Metabolism of Prematurity. III. Metabolism Findings in Twenty-One Premature Infants, ibid. **26:**29 (July) 1923.

In the plotting of the curve and the dots no sexual differentiation has been made.

Length of Trunk.—Measurements of the trunk were taken from the upper end of the sternum to the top of the pubis.

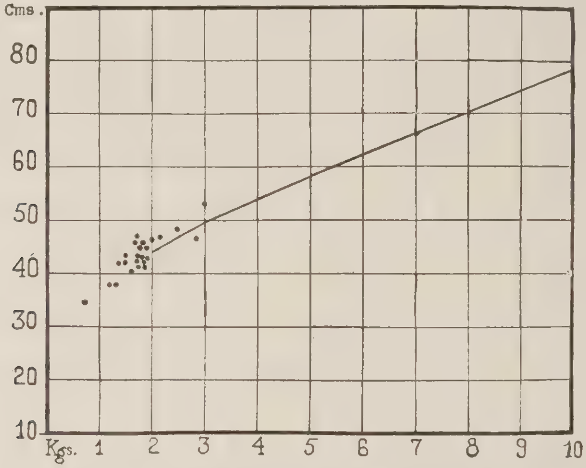

Chart 19.—Height referred to body weight.

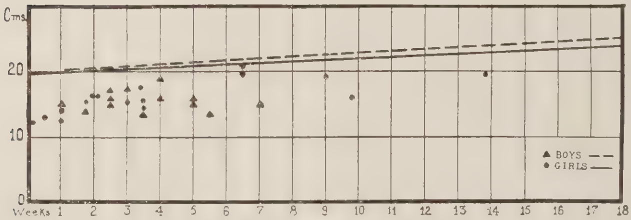

Chart 20.—Length of trunk.

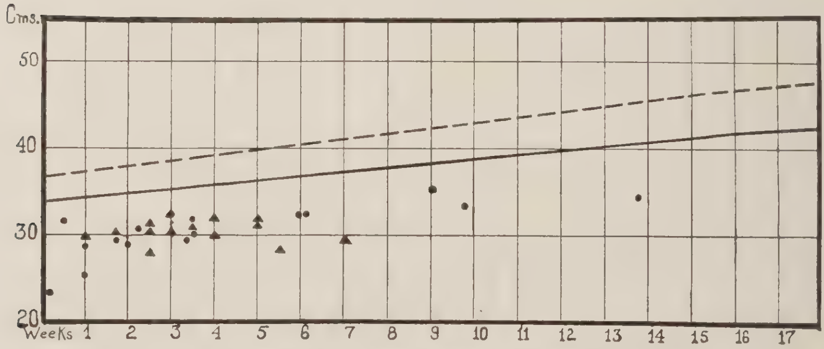

Chart 21.—Circumference of head.

Circumference of Head.—Measurements of the circumference of the head were taken over the occiput around the frontal bosses.

Circumference of Chest.—Measurements of the circumference of the chest were taken over the nipples, half way between full inspiration and expiration.

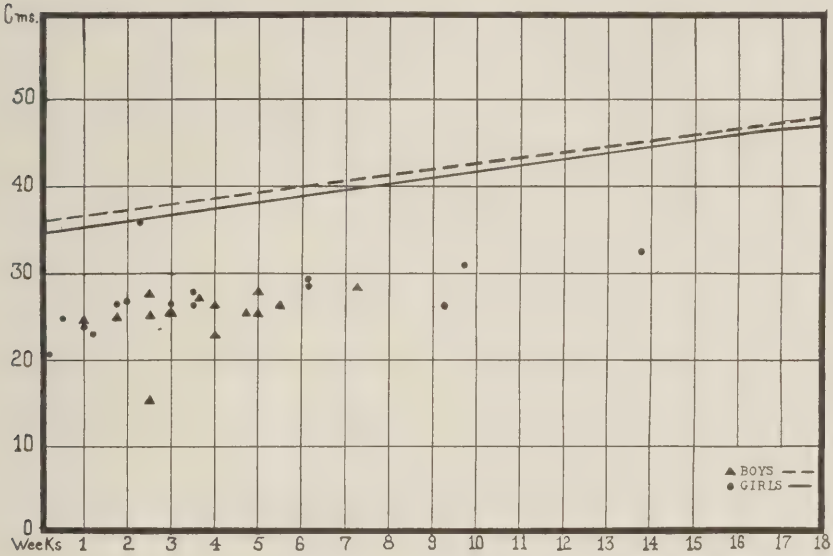

Chart 22.—Circumference of chest.

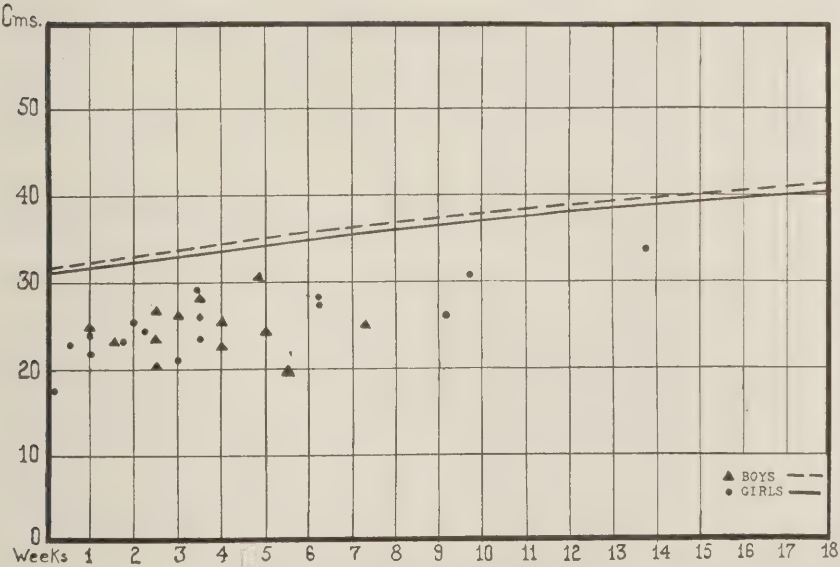

Chart 23.—Circumference of abdomen.

Circumference of Abdomen.—Measurements of the circumference of the abdomen were taken over the umbilicus.

Chart 21 shows that the circumference of the head of premature infants is closer to the normal than that of the chest or abdomen. This relation persists for several weeks after birth, and agrees with Ylppö's [9] findings that at birth the circumference of the head of premature infants is greater than that of the chest, while in full-term infants the circumferences are similar. He also showed that the greater the prematurity the more marked is the disproportion between the circumference of the head and chest. It has been difficult to confirm this in our series because of the uncertainty of the time of expected birth.

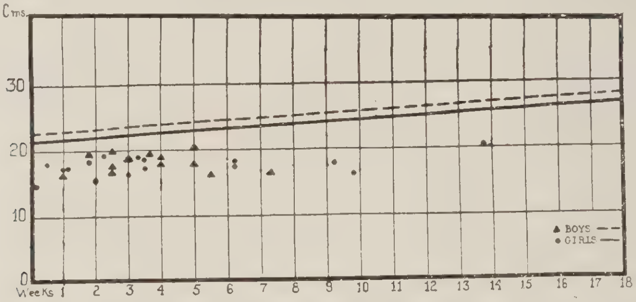

Chart 24.—Length of arms and hands.

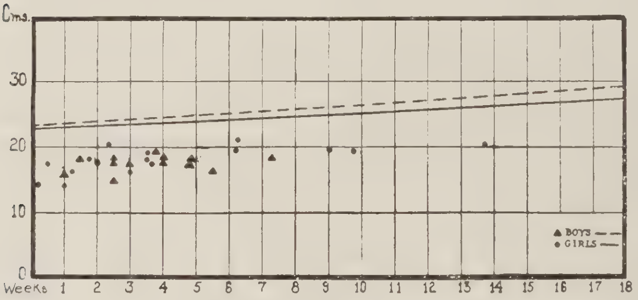

Chart 25.—Length of legs.

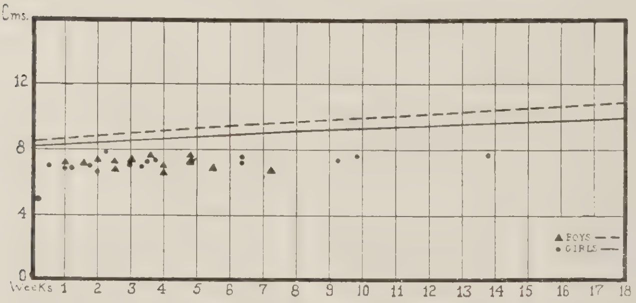

Chart 26.—Length of foot.

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[9] Ylppö: Ztschr. f. Kinderh. **24**:110, 1919.

Length of Arms and Hands.—Measurements of the arms and hands were taken from the tip of the acromion process to the end of the second finger.

Length of Legs.—Measurements of the length of the legs were taken from the top of the pubis in the mid-line to the bottom of the foot.

Length of Foot.—Measurements of the length of the foot were taken from the heel to the tip of the great toe.

The outstanding feature in the comparison of body measurements of premature infants with normal infants is that the premature infant is smaller at birth in all respects. This condition persists for many months after birth. No figures are available to show when the premature infant enters the normal zone. A premature infant, seen in private practice, who had been fed on breast milk, and was living in the most hygienic surroundings, was measured at 16 months and found to be within the normal limits. Another infant, seen in hospital practice, living in relatively poor surroundings, and fed with breast milk only for the first few weeks, had not reached normal at 17 months. In the opinion of many pediatricians, it takes a premature infant from 1 to 6 years to reach normal. It seems probable that much depends on how premature the infant is, whether it receives breast milk or not, and whether it escapes intercurrent infections and upsets during the first year of life.

Hess [10] in his treatise on prematurity has compiled data from many sources which emphasize the relation between the maturity and the weight and height of these infants. In general, the greater the prematurity the more marked is the deviation of the height and weight from the normal. The measurements correspond roughly with those of normal fetuses of the same maturity.

CONCLUSIONS

It is possible that the foregoing measurements, together with the available signs of prematurity, may be of diagnostic value in uncertain cases of prematurity. Whether such measurements are characteristic of prematurity alone it is impossible to say until measurements of other conditions, such as congenital weakness in new-born infants, etc., are obtained for comparison. Up to date, I have found no condition which invalidates the presumption that these deviations from the normal are characteristic of prematurity.

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10. Hess, J. H.: Premature and Congenitally Diseased Infants, Philadelphia, Lea & Febiger, 1922.

LOGARITHMIC CHARTS IN PEDIATRICS *

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For some considerable time I, like many other pediatricians, have been dissatisfied with the charts in general use at the present time, because they represent the absolute changes only of the conditions which we intend to record graphically, but fail to represent these in their relative, or better percentages of values.

Let us take, for instance, the growth charts for normal and healthy infants taken from the chapter on growth by Robertson,[1] and we shall see that one group of male infants, whose weight at birth was 5 pounds 6 ounces (2,438 gm.), will weigh 14 pounds 2 ounces (6,407 gm.) at the completion of the first year; a second group whose weight at birth was 6 pounds 4 ounces (2,841 gm.) will weigh 16 pounds 6 ounces (7,433 gm.) at the completion of the first year; a third group which he calls the standard average, whose weight at birth was 7 pounds 4 ounces (3,289 gm.), will weight 19 pounds 2 ounces (9,675 gm.) at the completion of the first year; a fourth group whose weight at birth was 8 pounds 4 ounces (3,742 gm.) will weigh 21 pounds 10 ounces (9,809 gm.) at the completion of the first year; and finally a fifth group, whose weight at birth was 9 pounds 8 ounces (4,309 gm.), will weigh 24 pounds 12 ounces (11,226 gm.) at the completion of the first year.

If we trace these weights on the ordinary charts now in common use, the same as Robertson's (Chart 1), then we shall get the impression that the development of a male infant is the more rapid and, therefore, the more favorable the greater its birth weight.

Practically the same is true for female infants (Chart 2).

Let us, however, trace these same weights on logarithmic charts, of which extensive use is made at the present time in the industries, where production, cost and other important items are to be expressed in percentages, and we shall at once observe that the rate of growth of these groups of infants runs parallel and that, therefore, their development is identical, no matter what their weight at birth, provided naturally that it has not been influenced by intercurrent diseases; and we also see that it is immaterial at which point of the chart we register our birth weights (Charts 3, 4 and 5).

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* Received for publication, Feb. 27, 1924.

[1] Robertson, T. B.: Abt's Pediatrics, Philadelphia, W. B. Saunders Company, 1923.

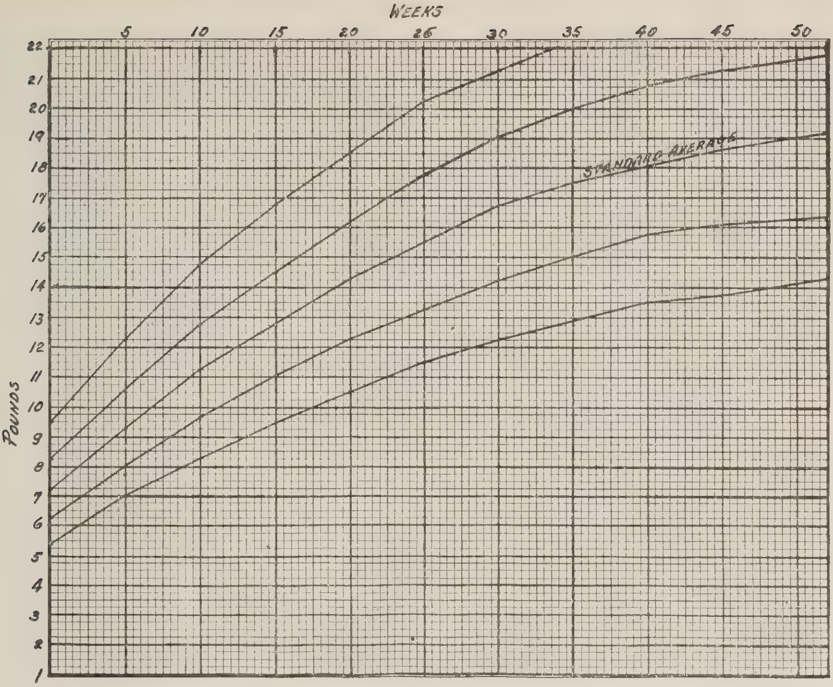

Chart 1.—Growth chart for male infants (Robertson).

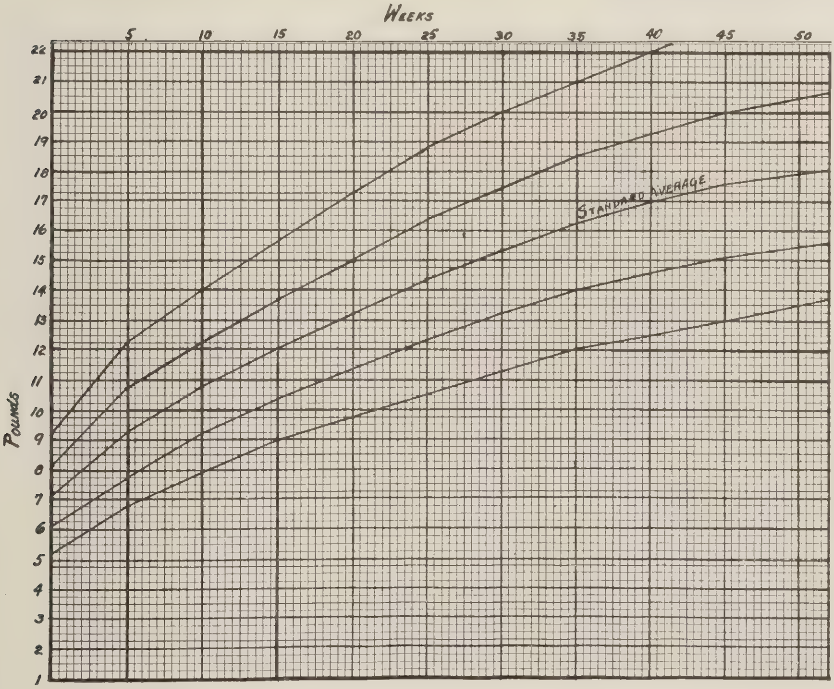

Chart 2.—Growth chart for female infants (Robertson).

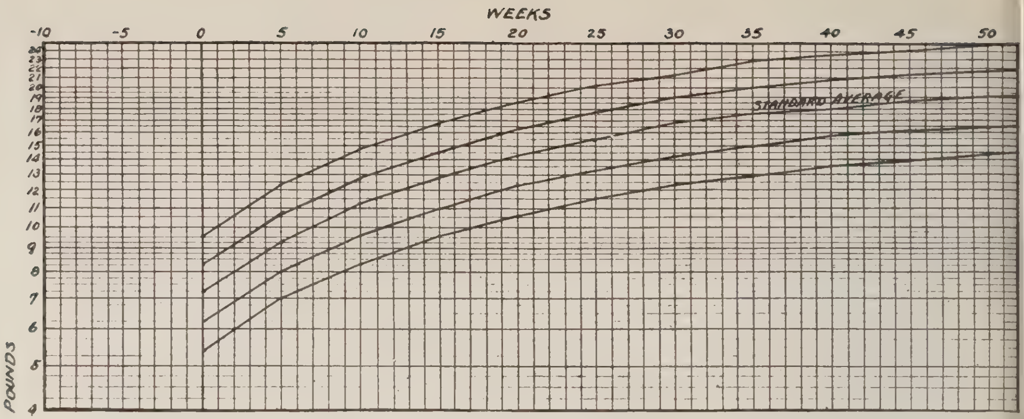

Chart 3.—Logarithmic chart, showing growth rate for male infants.

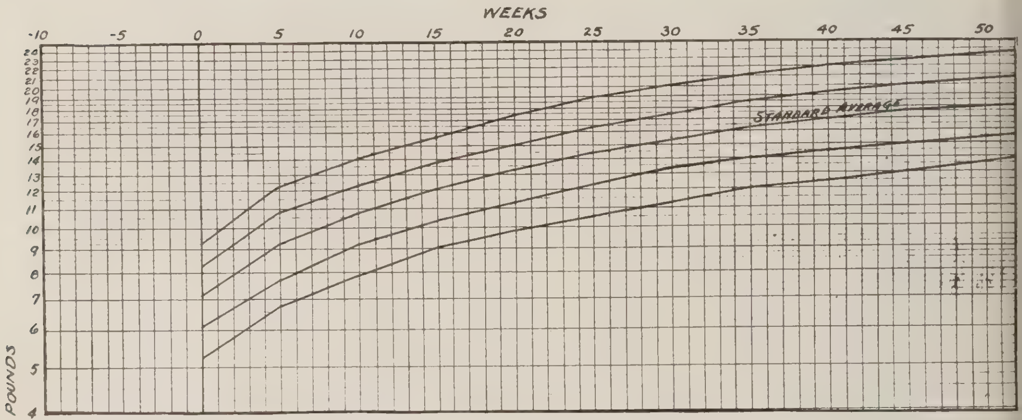

Chart 4.—Logarithmic chart, showing growth rate for female infants.

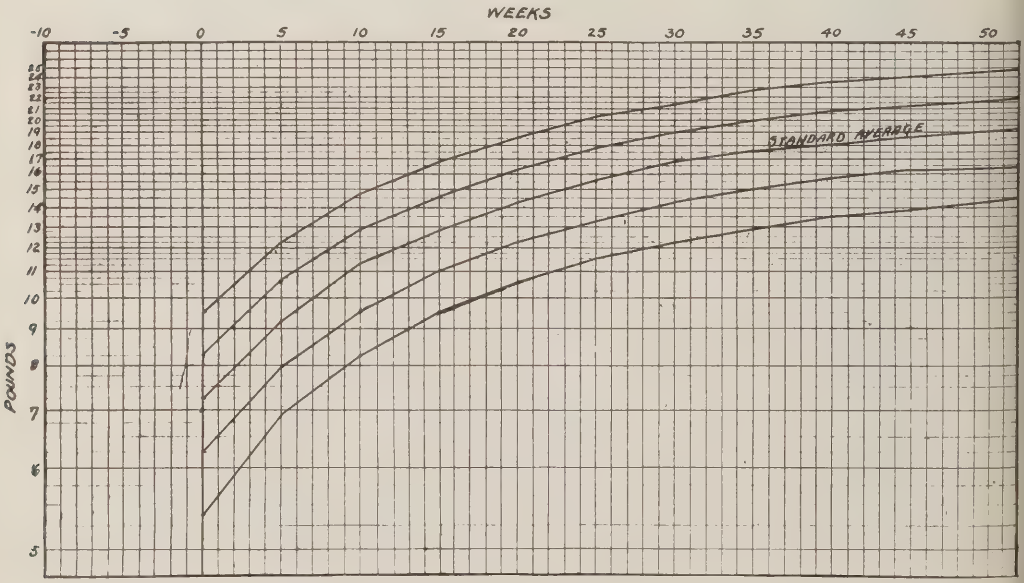

Chart 5.—Same as Chart 3.

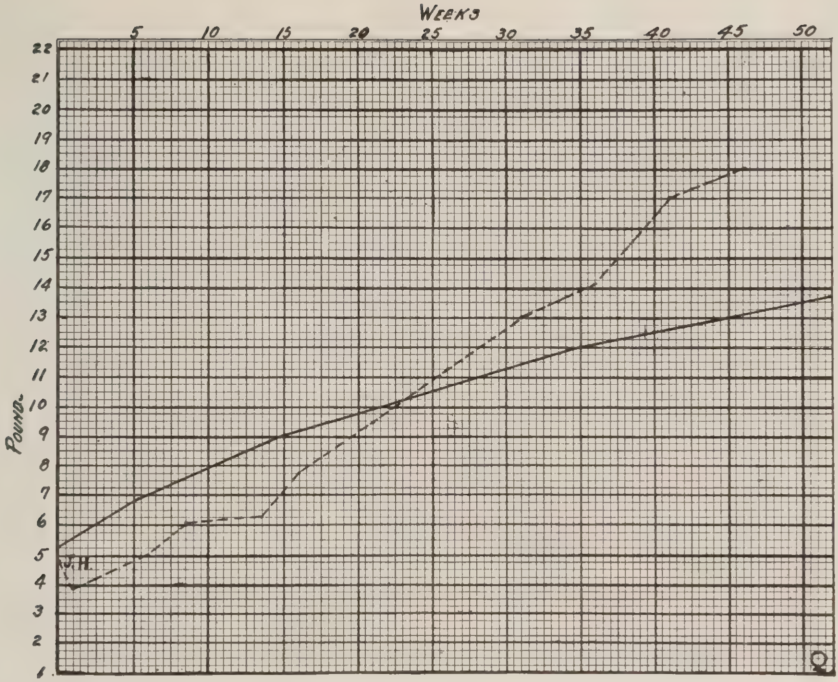

Chart 6.—Growth rate of female premature infant (broken line) compared with normal infant (straight line).

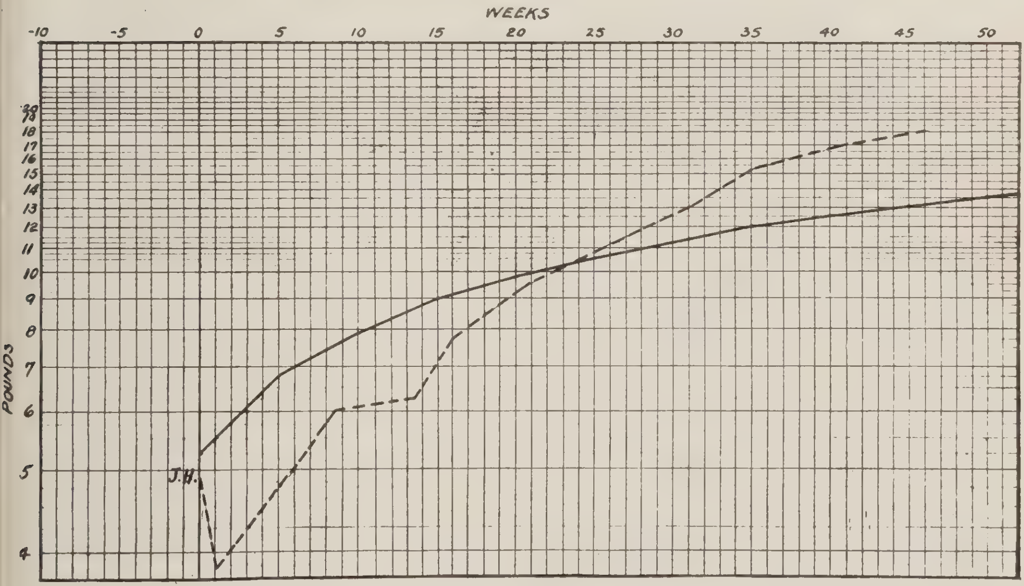

Chart 7.—Growth rate of same infants on logarithmic chart.

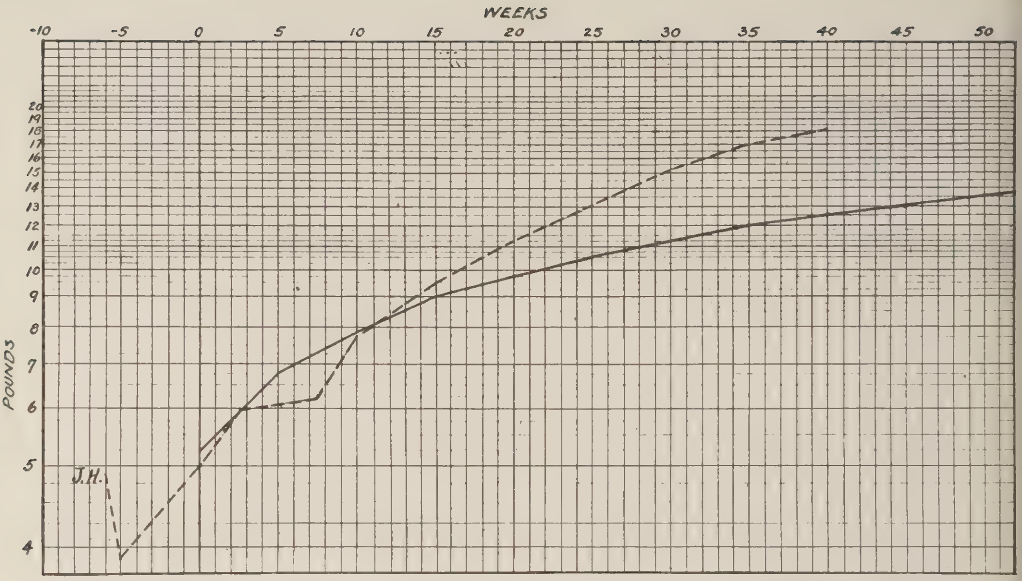

Chart 8.—More rapid development of prematurely born infant (broken line) than of normal infant (straight line).

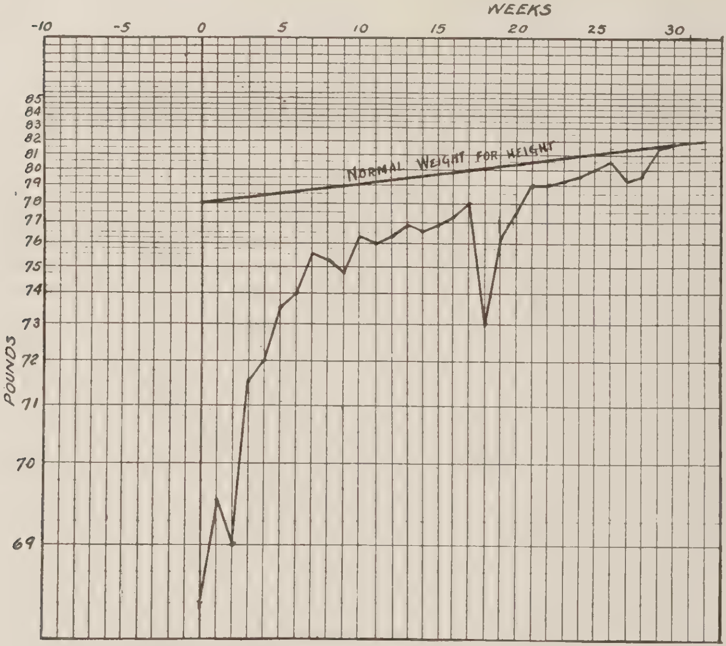

Chart 9.—Logarithmic chart of so-called "pretubercular" child.

The importance of recording the percentages of growth will be still more evident when we have to deal with infants whose weight at birth was abnormally low, due either to congenital debility or to premature birth; take, for instance, the weight chart of one of my little patients, J. H., who, though perfectly healthy, was born six weeks prematurely, and trace her weight on one of the charts now commonly in use together with that of a normal infant whose weight at birth was 5 pounds 4 ounces (2,381 gm.) (Chart 6) and compare these weights with a logarithmic chart (Chart 7) and we shall see that, according to the logarithmic chart the development of the premature infant (J. H.) was more favorable than that of the normal infant up to the thirty-fifth week of intra-uterine life, but that afterward the rate of development was about the same as that of the normal infant.

In drawing these charts of the prematurely born infants we do not, however, take into account the handicap under which the premature infant is laboring when we compare its rate of development with that of a normal infant born at term; in the former the physiologic birthday will fall on the day it should have been born if carried to full term, in the case of my patient (J. H.) six weeks after actual birth, while in the normal infant born at term the actual and the physiologic birthday are indentical.

I have, for this reason, placed the physiologic birthday on my logarithmic charts at zero, and I have left space to record the actual birth of prematurely born infants to the left of this zero, up to ten weeks, that is, up to where we may expect to have a viable fetus, so that in the case of my patient the actual birthday would be recorded at minus 6 weeks; we shall then see that, with the exception of a set back between the eighth and fourteenth week of her life, or between the second and eighth week after her physiologic birthday, the development of this prematurely born infant was much more rapid, when expressed in percentages, than that of her normal control (Chart 8).

In order to show that these charts are applicable to older children as well, I have recorded the chart of a so-called "pretubercular" child on one of my logarithmic charts (Chart 9); this chart was taken from Emerson's book.[2]

Further uses for these logarithmic charts can be developed with their employment. They may be readily prepared in any size desired with the aid of an ordinary slide rule; the originals for the charts here copied are size 6¾ by 10⅛ inches (15.6 by 25.4 cm.), as I have found this size most advantageous after extensive experiments. They can be copied at a nominal expense by photostat.

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2. Emerson, W. R. P.: Nutrition and Growth in Children, pp. 126 and 127, New York, D. Appleton & Company, 1922.

REPORT OF A CASE OF GANGRENE OF LEGS FOLLOWING BRONCHOPNEUMONIA *

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This case is of special interest for three reasons; first, because of the infrequency of gangrene of the extremities following pneumonia; second, because the gangrene occurred in both legs at about the same time and to the same extent; third, because the emboli causing the gangrene were located in about the same place in the popliteal arteries.

After reviewing the literature on this subject, several causes are given for gangrene in children, namely, burns,[1] local actions of chemicals, diseases of the nervous system (Raynaud's disease), constitutional diseases (hemophilia, purpura, and diabetes), thrombosis and embolism, and gangrene following measles, scarlet fever, diphtheria, varicella, erysipelas and typhoid fever. I was unable to find a single case of bilateral gangrene following pneumonia.

As to the frequency of gangrene, Frenkel[2] after reviewing the literature found fifty cases on record following measles, diphtheria, syphilis, and other infectious diseases. Two of the cases followed pulmonary tuberculosis and only one case was bilateral.

Bull,[3] in 6,140 necropsies, found six cases of gangrene in legs caused by emboli in the main arteries; bilateral in two cases.

Kiely[4] reported a case of gangrene of the fingers of both hands caused by sclerosis of brachial arteries.

Michael[5] reported a case of gangrene of the fingers of both hands caused by obliterative arteries.

Thorp[6] reported a case of gangrene of the toes of the left foot following measles and bronchopneumonia. In this case the gangrene extended upward to the middle third of left leg, and also occurred in the right great toe before death.

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* Received for publication, March 8, 1924.

* From the department of pediatrics, University of Georgia Medical Department.

[1] Cutler, G. D.: Gangrene of Toes in an Infant, Due to Scald, Am. J. Dis. Child. **21**:312 (March) 1921.

[2] Frenkel, H.: Original Article: Spontaneous Gangrene of Feet in Two Children, Ztschr. f. Kinderh. **29**:213 (June 3) 1921; abstr., J. A. M. A. **77**:500 (Aug.) 1921.

[3] Bull, P.: Emboli and Embolic Gangrene, Acta Chir. Scand. **54**:315 (Jan. 17) 1922; abstr., J. A. M. A. **78**:855 (March 18) 1922.

[4] Kiely, C. E.: J. Lab. & Clin. Med. **3**:352 (March) 1918.

[5] Michael, May: Case of Purpura with Symmetrical Gangrene of the Fingers, Am. J. Dis. Child. **20**:124 (Aug.) 1920.

[6] Thorp, E.: Lancet **2**:754 (Oct. 8) 1921.

Gordon[7] reported a case of gangrene of both feet following diphtheria.

Munk[8] reported two cases of gangrene in children. The first case had gangrene of the fingers of the left hand following measles and bronchopneumonia. The toxic infectious arteritis was thought to be the cause of gangrene. The second case was gangrene of the foot following the grip.

REPCRT OF CASE

History.—N. R., a negro boy, aged 6 years, entered the University Hospital on Aug. 2, 1922. The chief complaint at this time was pain in the epigastrium, disturbance in speech and tachycardia.

The patient had been sick for the last month. The trouble began with a sore throat after swimming. The cervical glands on the right side of the neck soon became swollen, the voice became nasal and there was also some swelling of the face. The child had been feverish every day.

Family History.—The father, mother and one brother were living and well. The mother had had four miscarriages before the birth of this child. There was no tuberculosis, nephritis or insanity in family.

Past Medical History.—The labor had been normal, the infant was breast fed for nine months, and had always been a healthy child. He had diphtheria at 3 years of age, epistaxis off and on all his life, and peeling of the skin on the palms of the hands and soles of the feet soon after birth. There was no history of snuffles.

Physical Examination.—The patient was a negro boy, emaciated and restless, who complained of shortness of breath. The temperature was 101; the pulse 130, and respiration 36.

The head was of normal shape; eyes, ears and nose normal; the throat not congested; the tonsils were enlarged; the voice had a nasal sound; all the neck veins were distended; the postcervical lymph glands were enlarged; dentition was fair.

The thorax showed rapid respiration with an expiratory grunting sound; the respiratory movements were shallow and about equal on both sides. There was some dulness over both bases posteriorly; a few fine crackling râles were heard over the left base posteriorly and the breath sounds were slightly tubular over the left base posteriorly. Rhonchus was present over the entire chest in front.

The heart was enlarged to the right and left, the pulmonic second sound was accentuated; there was a booming first sound, no thrill was present, a systolic murmur was heard over the entire pericardium and also heard in the left axilla. The point of maximum intensity was at the pulmonic area.

The abdomen was distended, the liver enlarged, its edge palpable six finger breadths below the costal margin in the nipple line; the spleen and kidneys were not palpable.

The extremities showed no edema of the legs, but a slight stiffness of the right ankle.

The epitrochlea and postcervical glands were enlarged.

Roentgenogram of the chest showed a greatly enlarged heart, with no evidence of fluid in either pleural cavity. Both lungs were infiltrated.

Laboratory Findings.—Blood: the white blood count was 22,000, red count, 2,700,000, hemoglobin 50 per cent., malaria smear negative, differential count showed 70 per cent. polymorphonuclears, large lymphocytes 4 per cent., small lymphocytes 26 per cent., blood platelets, 296,000, coagulation time, five minutes.

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[7] Gordon, U. B., and Newman, B.: Report of a Case of Gangrene of the Feet Following Diphtheria, Am. J. Dis. Child. **23**:142 (Feb.) 1922.

[8] Munk: Arch. Med. des Enf. **1**:434, 1898.

The Wassermann test was negative; the sputum negative; the throat culture negative for diphtheria bacillus.

The urine showed albumin three plus, sugar negative, microscopic examination showed a few hyaline and granular casts and pus cells.

Diagnosis at this time was as follows: Bronchopneumonia, cardiac dilatation and hepatic and renal congestion.

On August 9, the thirteenth day in hospital, the patient had a temperature of 100, pulse 120, respiration 26. Examination of the legs showed definite gangrene, dry type, involving all the toes on the left foot. He also had gangrene beginning in all the toes on the right foot. The pulse in the left dorsalis pedis artery was slightly diminished; a normal pulse was obtained in the right dorsalis pedis artery. The patient at this time complained of tenderness and pain in both legs.

On August 15, two days later, the patient had a temperature of 100, pulse 118, respiration 28. White blood count 18,000; urine negative.

The lungs at this time were clear. The heart was normal in size and no murmurs were audible.

The abdomen was negative. The patient showed marked emaciation, and kept his legs flexed on the thighs and the thighs flexed on his body. He complained of severe pain in both legs and knees when legs were extended. Gangrene had extended to the middle third of both legs and a line of demarkation was present on both sides. No femoral or popliteal pulse could be palpated. A roentgenogram of both legs did not show any arterial occlusion. Amputation of both legs above the knees was advised by the surgical staff at this time.

On September 26, both legs were amputated above the knees by Dr. Chaney. After operation, the patient gained weight and was discharged from the hospital as "well," on Nov. 2, 1922.

The pathologic report was as follows: Embolic blocking by portion of thrombus of both popliteal arteries. Gangrene of both feet and lower two-thirds of legs. The gangrene of the feet was the dry type; that of the legs was the wet type. The embolus in the right popliteal artery was lodged at the origin of the anterior tibial artery; that in the left popliteal artery was a little higher up behind the knee.

POSTENCEPHALITIC BEHAVIOR DISTURBANCE WITHOUT PHYSICAL SIGNS *

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AND
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It has been generally recognized that postencephalitic mental disturbances in children are always preceded by some physical signs. Behavior disturbances, recognized as due to the encephalitis, because of an acute onset following a typical epidemic encephalitis history, are nearly always accompanied by some neurologic findings in the form of pupillary changes, facial paresis, muscle stiffness, etc. These behavior disturbances have been shown to be typical of an organic brain disease quite unlike the usual behavior disturbances in children. It has been demonstrated [1] that there is little or no correlation between the severity of the mental disturbance and the physical symptoms; children with slight mental disturbance may have extreme physical findings and vice versa.

Originally the behavior of a child was pronounced postencephalitic when the following three conditions were fulfilled: (1) a sudden change in personality, (2) physical evidence of postencephalitis and (3) a history of acute epidemic encephalitis. Later the third factor was not considered essential, since typical postencephalitic syndromes were frequently found without any history of an acute illness.

Children with postencephalitic behavior disturbances, however, present so typical a picture to the psychiatrist that he is often tempted to make the diagnosis even in the absence of physical findings. Since our last publication we have had under observation two children [2] presenting typical "postencephalitic behavior disturbances," in whom the physical signs appeared long afterward as typical parkinsonian syndromes; in one case, six months, and in the second case, two years after the original examination. The problem was first brought to our attention in the cases presented.

REPORT OF CASES

Case 1.—John, a boy, aged 11 years, was referred by the Juvenile Court in January, 1923, because of "disobedience, lying, fighting, stealing and cruelty to children and animals." He was said to be "entirely uncontrollable, both at home

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* Received for publication, April 2, 1924.

[1] Sherman, M., and Beverly, B. I.: Deterioration in Children Showing Behavior Difficulties Following Epidemic Encephalitis, Arch. Neurol. & Psychiat. **10**:329-340 (Sept.) 1923.

[2] Seen at the Institute for Juvenile Research, State of Illinois, Department of Public Welfare.

and in school." This behavior began in November, 1922, about three years after an illness, during which "he slept a considerable part of the time over a period of four or five weeks." A more adequate medical history could not be obtained. The behavior disturbance dated from the illness, but until November, 1922, only an increased irritability was noted.

Examination revealed a sluggish, apathetic appearing, but well developed and nourished boy who did not appear ill. He admitted his delinquencies readily, but could give no reason for his behavior. He had little insight into his difficulties, and appeared to have little control over his conduct. He was very shallow emotionally, and appeared entirely indifferent to the examination or his difficulties. By the Stanford-Binet intelligence tests he was found to have a mental age of 8 years and 10 months; intelligence quotient, 78. He was classified in the high borderline group. The neurologic examination was entirely negative.

In this patient, a sudden change in personality developed about three years after an illness, presumably epidemic encephalitis. The behavior and the mental symptoms being similar to that observed in a large series of postencephalitic children, a diagnosis of "probable postencephalitic behavior disturbance" was made.

Six months later the boy returned for a second examination. The behavior was unchanged. The psychologic examination revealed no evidence of a mental deterioration. The psychiatric findings were similar to those noted at the time of the first examination. The neurologic findings, however, were: slow gait; left arm immobile and slightly flexed when walking; a masked expression; unequal, irregular, sluggish pupils; tremor of the fingers. None of these findings was present at the time of the first examination. There was no history of an intervening illness.

Case 2.—James, a boy, aged 15 years, was first examined in June, 1921. He was referred by the Board of Education with the following history. Until September, 1920, he was never considered a school problem; since that time he was reported to the principal of the school several times for indecent exposures. "He was incorrigible, and a great nuisance to the teachers." By the Stanford-Binet intelligence examination he was found to have a mental age of 11 years and 6 months; intelligence quotient, 86. The psychiatric examination revealed chiefly emotional shallowness and instability. He did not deny the behavior in school, but could give no reason for his conduct. His behavior appeared very childish for a boy with his mental age. The medical history, with the exception of frequent colds, was entirely negative. The pupils were slightly irregular, unequal and sluggish. The physical examination was otherwise negative. Because of the pupillary findings, a tentative diagnosis of syphilis of the central nervous system was made. The blood Wassermann was negative. A spinal puncture was advised but not performed.

Two years later the patient was returned by the Juvenile Court for a second examination. There was little or no change in his behavior. However, he now appeared very dull; the expression was mask-like and for this reason he was diagnosed as feebleminded by a local physician. By mental tests, however, his mental age was found to be 15 years, 4 months, intelligence quotient, 99, indicating adequate intelligence. There was no evidence of deterioration in intelligence. The psychiatric examination revealed a dull, emotionally shallow boy having little insight into his situation and unable to give any explanation for his delinquencies. The physical examination now gave clear-cut evidence of a postencephalitic syndrome. There was a slow, stiff gait; a masked expression; markedly unequal, irregular, sluggish pupils; gross tremor of the fingers; facial paresis, and a cogwheel resistance in the extremities. These findings were not present at the time of the first examination, excepting the pupillary changes which were now much more evident. The blood Wassermann was negative.

In a well developed case of behavior disturbance following epidemic encephalitis, there are both gross personality changes and distinct physical evidence of an organic brain disease. The explanation for marked personality changes preceding the physical signs is highly theoretical. From Bassoe's[3] analogy of postencephalitic syndromes with tertiary syphilis involving the central nervous system we may assume that the mental symptoms are the person's reaction to the toxic effects of the disease virus before the onset of degenerative changes. Bassoe states (in comparing syphilis to encephalitis) that "The most interesting point connecting these two diseases is the apparent existence in encephalitis as well of a 'para' stage, i. e. of progressive cerebral diseases coming on after the acute illness, and separated from it by an apparently normal interval. This is particularly true of postencephalitic parkinsonian syndrome. . . . The view is gaining ground that the virus, like that of syphilis, may remain dormant for years, and then give rise to a more chronic and degenerative process than the one encountered in the typical disease." Nonne[4] is evidently of the same opinion. He "attributes the various symptoms (postencephalitic) to the presence of a special toxin that affects the nervous centers very much like the metasyphilitic toxin." Other explanations would be that the mental symptoms result from degenerative changes that produce no immediate neurologic signs; that they are due to repeated mild infections productive of no clinical findings, or that they are due to a very chronic stage of the original acute infection.

COMMENT

A sufficient number of postencephalitic behavior disturbance cases have been studied to enable us to recognize a fairly constant symptomatology. A history of influenza or an undiagnosed condition with diplopia, a permanently developed strabismus, or a protracted period of somnolence is frequently obtained and should immediately arouse suspicion. The mental and personality changes may date from the illness or develop after a period of time even to several years. Personality changes manifested by a change in disposition, inability to sleep at night, violent outbursts of temper, irresponsibility, incorrigibility in school, hindrance in school work, cruelty to animals, lying, etc., are the most frequent complaints. The delinquencies are nearly always committed alone and are influenced but slightly by changes in environment. Deterioration of intelligence, poor memory and poor attention are often reported by teachers and parents. The psychologic examination, however, gives no evidence of deterioration in intelligence. The attention and other mental capacities are normal, except for changes due to the emotional disturbance. The general impression after observing their behavior in the examining room is that the intelligence is low. The childish mannerisms, impulsive nature of the delinquencies, poor insight into their mental difficulty, the appearance of deterioration, are in marked contrast with the high rating obtained by intelligence tests. This, we think, is the most outstanding characteristic. Moreover, all these findings are referred to a definite time of onset. In a large percentage of children there is hyperactivity, irritability, alertness and marked emotional instability, the emotional tone varying from extreme anger to a cordial attitude within a few seconds. In a much smaller percentage (two of twenty cases in our first series) there was a marked indifference, lack of initiative, and sluggish bodily activity. Often there is paroxysmal polypnea with the emotional outbreaks. In one case (in a series of forty cases) there was mental difficulty manifested by extremely slow comprehension. In another case marked weakness of the lower extremities was the initial complaint.

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[3] Bassoe, Peter: The Diagnosis of Epidemic Encephalitis, J. A. M. A. **79**:2223 (Dec. 30) 1922.

[4] Nonne: Extracts, Congress of the German Society for Internal Medicine, Vienna, April, 1923, abstr. J. A. M. A. **80**:1629 (June 2) 1923.

CONCLUSION

Even in the absence of definite neurologic findings or a history of an acute disease, or both, when a child shows a sudden change of personality and symptoms of impulsive delinquencies and childish mannerisms, the appearance of deterioration in contrast with a high mental test rating, explosive reaction, with general hyperkinesis and irritability, or marked indifference with sluggish physical reactions, the possibility of an organic brain disease, especially postencephalitis, should be considered.

A COMPARISON OF THE METABOLISM OF SOME MINERAL CONSTITUENTS OF COW'S MILK AND OF BREAST MILK IN THE SAME INFANT *

II. CHLORID METABOLISM

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Chlorid metabolism experiments were conducted at the same time as those on calcium, previously reported,[1] and on the same subjects. We were unable to find that any work has been done with breast milk and cow's milk, using the same infant as subject. The literature on chlorid metabolism, therefore, deals with different subjects on a breast milk diet and others on a diet with cow's milk. Blauberg [2] compared the relative utilization of chlorid in diluted and undiluted cow's milk with that of breast milk. He used one subject for each kind of milk, and found the highest utilization in breast milk, 93.1 per cent. With undiluted cow's milk the figure was 81.8 per cent. and with modified cow's milk 59.4 per cent. He found that chlorids were utilized more completely than any other of the minerals.

Hoobler [3] calls attention to the fact that sodium chlorid has the most varied and important functions to perform, such as the maintenance of osmotic pressure and the regulation of the retention and excretion of water. The utilization is usually above 90 per cent. of the intake in both kinds of milk, according to this investigator, while the retention of sodium chlorid is only sufficient under normal conditions to cause a balance to be maintained in the body fluids. Chlorid excretion takes place almost entirely through the urine, the amount usually running about 2 gm. daily, whereas only 0.1 gm. daily is excreted through the

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* Received for publication, March 8, 1924.

* From the Sarah Morris Hospital for Children, the Gusta Morris Rothschild Fund of the Michael Reese Hospital and the Nelson Morris Memorial Institute for Medical Research.

1. Wang, C. C.; Witt, D. B., and Felsher, A. R.: A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant. I. Calcium Metabolism, Am. J. Dis. Child. **27:** (April) 1924.

2. Blauberg, M.: Experimentelle Beiträge zur Frage den Mineralstoffwechsel beim künstlich ernährten Säugling, Ztschr. f. Biol. **40:**1, 1900; Ueber den Mineralstoffwechsel beim natürlich ernährten Saugling, Ztschr. f. Biol. **40:**36, 1900.

3. Hoobler, B. R.: The Rôle of Mineral Salts in the Metabolism of Infants, Am. J. Dis. Child. **2:**107 (Aug.) 1921.

feces. Baumgarten[4] reports that the sodium chlorid excretion is independent of the intake, but he worked with pathologic subjects. Freund[5] on the other hand, finds that sodium chlorid excretion cannot be considered apart from the intake.

Description of Experiment.—The excretions were prepared as described in the previous paper.[1] For the determinations of sodium chlorid in feces, about 0.5 gm. of the dried and powdered feces was used. This was weighed into a silicon crucible, 2 c.c. of 5 per cent. sodium carbonate was added, and the material dried and ignited at a dull red temperature for one hour in an electric furnace. The ash was taken up in hot water and the chlorid precipitated with standard silver nitrate. The excess of silver nitrate was titrated against standard ammonium thiocyanate, using ferric ammonium sulphate as indicator. This, with some modifications, is the official method of the agricultural chemists for chlorids in beef extract.[6]

For chlorids in urine the method outlined by Harvey[7] was used without modification. The chlorids were precipitated with standard silver nitrate, and the excess of silver nitrate titrated against standard ammonium thiocyanate, using ferric ammonium sulphate as indicator.

The method developed by Denis and Sisson[8] was used with some modification for the determination of the chlorin intake in milk. To 10 c.c. of the milk 20 c.c. of 1.2 per cent. picric acid and 20 c.c. of standard silver nitrate were added, and the whole was centrifuged for five minutes. To 10 c.c. of the clear supernatant liquid was added 2 c.c. of ferric ammonium sulphate as indicator, and the excess of silver nitrate was titrated against standard ammonium thiocyanate. The experiments were made in triplicate and the results averaged.

COMMENT

It will be seen from Table 1 that although there is not always a close check in the chlorid content of the feces, the daily variation in chlorid utilization is not very great, since most of the chlorid is eliminated through the urine, as Hoobler[3] has also found. For convenience in comparison with the work of others the averages of the three-day periods are used as given in Table 2.

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[4] Baumgarten, O.: Ueber "organisch" gebundenes Chlor im Harn, Zeit. f. exp. Path. u. Therap. **5**:540, 1908-1909.

[5] Freund, W.: Chlor und Stickstoff im Säuglings-organismus, Jahrb. f. Kinderh. **48**:137, 1898.

[6] Bureau of Chemistry Bulletin 107 (Revised), U. S. Department of Agriculture, 1912, p. 114.

[7] Harvey, S. C.: The Quantitative Determination of the Chlorids in the Urine, Arch. Int. Med. **6**:12 (July) 1910.

[8] Denis, W., and Sisson, W. R.: A Study of the Chlorin Content of Milk and Blood After the Ingestion of Sodium Chlorid, J. Biol. Chem. **46**:483 (May) 1921.

Table 1.—*Daily Chlorid Metabolism in Healthy Infants Fed on Breast Milk and Cow's Milk*

			NaCl Intake		NaCl Output				NaCl Utilization			NaCl Retention		
Name	Kind of Milk	Date	Per 24 Hours, Gm.	Per Kg., Gm.	Feces per 24 Hours, Gm.	Urine per 24 Hours, Gm.	Total per 24 Hours, Gm.	Total per Kg. per 24 Hrs., Gm.	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake
W. O.	Breast	11/26/21	0.4036	0.0977	0.0806	0.2566	0.3372	0.0816	0.3230	0.0782	80.02	0.0664	0.0161	16.45
		11/27/21	0.4036	0.0977	0.1416	0.1878	0.3294	0.0798	0.2620	0.0634	64.91	0.0742	0.0180	18.38
		11/28/21	0.4109	0.0995	0.1156	0.1800	0.2956	0.0716	0.2953	0.0715	71.86	0.1153	0.0279	28.06
	Cow's	12/ 7/21	1.3010	......	0.1868	1.1251	1.3119	0.2988	1.1142	0.2537	85.58	—0.0109	—0.0025	.....
		12/ 8/21	1.3010	0.2964	0.0974	0.7218	0.8192	0.1866	1.2036	0.2743	92.52	0.4818	0.1097	37.02
		12/ 9/21	1.3010	......	0.1820	0.8166	0.9986	0.2275	1.1190	0.2548	85.96	0.3024	0.0689	23.23
	Breast	12/16/21	0.5456	......	0.0216	0.2282	0.2498	0.0560	0.5240	0.1175	96.03	0.2958	0.0663	53.73
		12/17/21	0.5456	0.1224	0.0713	0.2782	0.3495	0.0784	0.4743	0.1064	86.94	0.1961	0.0440	35.94
		12/18/21	0.5456	......	0.0826	0.2895	0.3721	0.0834	0.4630	0.1039	84.86	0.1736	0.0389	31.79
E. M.	Cow's	11/26/21	1.5420	0.2075	0.3388	2.0168	2.3556	0.3169	1.2032	0.1619	78.01	—0.8136	—0.1095	.....
		11/27/21	1.6400	0.2208	0.2937	0.9249	1.2186	0.1640	1.3463	0.1811	82.06	0.4214	0.0567	25.70
		11/28/21	1.6630	0.2238	0.2894	0.9110	1.2004	0.1616	1.3736	0.1849	82.66	0.4626	0.0623	27.83
	Breast	12/ 3/21	0.5334	0.0728	0.1890	0.3569	0.5459	0.0745	0.3444	0.0470	64.56	—0.0125	—0.0017	.....
		12/ 4/21	0.5334	......	0.0370	0.3586	0.3956	0.0540	0.4964	0.0677	93.08	0.1378	0.0188	25.84
T. O.	Breast	12/13/21	0.3816	......	0.0015	0.3577	0.3592	0.1009	0.3795	0.1066	99.63	0.0218	0.0061	5.72
		12/14/21	0.3816	0.1070	0.0015	0.3577	0.3592	0.1009	0.3795	0.1066	99.63	0.0218	0.0061	5.72
		12/15/21	0.3816	......	0.0182	0.4008	0.4190	0.1177	0.3628	0.1020	95.26	—0.0380	—0.0107	.....
	Cow's	1/14/22	1.4350	......	0.1305	1.0420	1.1725	0.2902	1.3045	0.3207	90.30	0.2625	0.0650	18.29
		1/15/22	1.4350	0.3551	0.1305	1.0420	1.1725	0.2902	1.3045	0.3207	90.30	0.2625	0.0650	18.29
		1/16/22	1.4350	......	0.0780	1.1834	1.2614	0.3122	1.3570	0.3359	94.58	0.1736	0.0430	12.10
B. N	Cow's	3/ 9/22	1.2323	......	0.0099	0.8942	0.9041	0.2773	1.2224	0.3749	99.20	0.3282	0.1007	26.65
		3/10/22	1.2323	0.3779	0.0330	0.8121	0.8451	0.2593	1.1993	0.3679	97.34	0.3872	0.1188	31.43
		3/11/22	1.2323	......	0.0137	0.7405	0.7542	0.2314	1.2186	0.3739	98.93	0.4781	0.1450	38.81
	Breast	3/30/22	0.3375	......	0.0207	0.2197	0.2404	0.0664	0.3168	0.0875	93.88	0.0971	0.0268	28.77
		3/31/22	0.3375	0.0932	0.0207	0.2197	0.2404	0.0664	0.3168	0.0875	93.88	0.0971	0.0268	28.77
		4/ 1/22	0.3375	......	0.0647	0.2379	0.3021	0.0834	0.2733	0.0755	81.00	0.0354	0.0098	10.49
B. B.	Cow's	2/25/22	1.5670	......	0.0352	1.0780	1.1132	0.2914	1.5318	0.4011	97.78	0.4538	0.1188	28.96
		2/26/22	1.5670	0.4102	0.0352	1.0780	1.1132	0.2914	1.5318	0.4011	97.78	0.4538	0.1188	28.96
		2/27/22	1.5670	......	0.0630	1.3151	1.3781	0.3607	1.5040	0.3937	95.96	0.1889	0.0495	12.06
	Breast	3/ 8/22	0.4477	......	0.0088	0.2888	0.2976	0.0746	0.4389	0.1100	98.04	0.1501	0.0376	33.53
		3/ 9/22	0.4477	0.1122	0.0168	0.3440	0.3608	0.0904	0.4309	0.1080	96.25	0.0869	0.0218	19.41
		3/10/22	0.4477	......	0.0247	0.4090	0.4337	0.1087	0.4230	0.1060	94.48	0.0140	0.0035	3.13
	Cow's	3/29/22	1.7400	......	0.0020	1.4065	1.4085	0.3172	1.7380	0.3913	99.88	0.3315	0.0746	19.05
		3/30/22	1.7400	0.3948	0.0559	1.3972	1.4531	0.3273	1.6841	0.3793	96.80	0.2869	0.0646	16.49
		3/31/22	1.7400	......	0.0559	1.3972	1.4531	0.3273	1.6841	0.3793	96.80	0.2869	0.0646	16.49
	Breast	4/11/22	0.4577	......	......	0.3631	......	......	......	......	.....	......	......	.....
		4/12/22	0.4577	0.0982	0.0037	0.8512	0.8549	0.1835	0.4540	0.0974	99.20	—0.3972	—0.0852	.....
		4/13/22	0.4577	......	......	0.3821	......	......	......	......	.....	......	......	.....

TABLE 2.—*Average Daily Chlorid Metabolism of Healthy Infants Fed on Breast Milk and Cow's Milk*

					NaCl Intake		NaCl Output				NaCl Utilization			NaCl Retention		
Name	Age, Mo.	Body Weight	Kind of Milk	Fat	Per 24 Hours, Gm.	Per Kg., Gm.	Feces per 24 Hours, Gm.	Urine per 24 Hours, Gm.	Total per 24 Hours, Gm.	Total per Kg. per 24 Hours, Gm.	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake
W. O.	2.6	4.13	Breast	4.0	0.4060	0.098	0.1126	0.2081	0.3207	0.078	0.2934	0.071	72.3	0.0853	0.021	21.0
	3.0	4.39	Cow's	...	1.3010	0.296	0.1554	0.8878	1.0432	0.238	1.1456	0.261	88.1	0.2578	0.059	19.8
	3.3	4.46	Breast	4.4	0.5456	0.122	0.0585	0.2653	0.3238	0.073	0.4871	0.109	89.3	0.2218	0.050	40.7
E. M.	5.5	7.43	Cow's	2.2	1.6150	0.217	0.3073	1.2842	1.5915	0.214	1.3077	0.176	81.0	0.0704	0.010	4.4
	5.7	7.33	Breast	3.8	0.5334	0.073	0.1130	0.3577	0.4707	0.064	0.4204	0.057	78.8	0.0626	0.009	11.7
T. O.	3.2	3.56	Breast	4.0	0.3810	0.107	0.0071	0.3721	0.3791	0.107	0.3739	0.105	98.1	0.0019	0.001	0.5
	4.3	4.04	Cow's	2.2	1.4350	0.355	0.1130	1.0891	1.2021	0.298	1.3220	0.326	92.1	0.2329	0.058	16.2
B. N.	0.4	3.26	Cow's	2.1	1.2323	0.378	0.0189	0.8156	0.8345	0.256	1.2134	0.372	98.5	0.3978	0.122	32.3
	1.4	3.62	Breast	3.6	0.3375	0.093	0.0352	0.2258	0.2610	0.072	0.3023	0.084	89.6	0.0765	0.022	22.7
B. B.	1.3	3.82	Cow's	2.0	1.5670	0.410	0.0445	1.1157	1.2015	0.315	1.5238	0.598	97.2	0.3655	0.096	23.3
	1.6	3.99	Breast	4.2	0.4477	0.112	0.0168	0.3473	0.3640	0.091	0.4309	0.108	96.2	0.0837	0.021	18.7
	2.1	4.44	Cow's	2.2	1.7400	0.395	0.0379	1.4003	1.4382	0.324	1.7021	0.383	96.1	0.3018	0.068	17.3
	2.4	4.66	Breast	3.4	0.4577	0.098	......	0.5321	......	.....	......	.....	....	......	.....	....

Difference in the Quantity of Chlorid Excretion in Feces and Urine Brought About by the Change of Milk.—The chlorid intake in our cases is invariably much greater on a diet of cow's milk than of breast milk; with cow's milk it varied from 1.2323 gm. to 1.7400 gm. per twenty-four hours, with an average of 1.4817 gm. The corresponding figures for breast milk are 0.3810 gm. to 0.5456 gm. with an average of 0.4441 gm. These figures are in general higher than those of other investigators. Table 3 shows figures reported by other investigators working on breast fed infants. The range here is from 0.1140 gm. to 0.4586 gm. per twenty-four hours. Table 3 also gives figures for cow's milk from three investigators. Blauberg[2] had a lower chlorid intake than ours, Hoobler[3] higher, but Tangle's[9] figures are much like ours.

A change from one milk to the other is always accompanied by a change in the chlorid excretion both in feces and in urine. With the exception of one case (B. N.), the value for feces is always higher for cow's milk than for breast milk. There is a great variation in different individuals in the sodium chlorid content of feces; with breast milk the values varied from 0.0071 gm. to 0.1130 gm. per twenty-four hours, with an average of 0.0572 gm. With cow's milk it ran from 0.0189 gm. to 0.3073 gm. with an average of 0.1128 gm. Other investigators show a range of sodium chlorid content in feces of from 0.0045 gm. to 0.1210 gm., which is even greater than ours. The four cases of cow's milk reported in Table 3 also show a marked variation, from 0.042 gm. to 0.1170 gm. There is no consistent relation between the intake and excretion of sodium chlorid in the feces, either in our work or in the previous work reported.

An increase of sodium chlorid intake leads to a decided increase in the output of sodium chlorid in the urine. Both are invariably higher on a diet of cow's milk and every change from breast milk to cow's milk brought about an increase in urinary sodium chlorid. The breast fed infants excreted from 0.2081 gm. to 0.5321 gm. urinary sodium chlorid per twenty-four hours, with an average of 0.3298 gm. With cow's milk the figures were 0.8156 gm. to 1.4033 gm., with an average of 1.0988 gm. In every case when the milk is changed the increase or decrease of urinary sodium chlorid is threefold or more. In the case of B. B., on whom the experiment was repeated with both diets, the excretion increased with age on breast milk and on cow's milk, although the intake per kilogram in the second period was lower both times. However, comparing different infants, there is no apparent relationship between age and the amount of urinary sodium chlorid.

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9. Tangle, Franz: Der Stoff und Energieumsatz eines künstlich ernährten Säuglings, Arch. f. d. ges. Physiol. **104**:453, 1904.

TABLE 3.—*Chlorid Metabolism in Healthy Infants Fed on Breast Milk and Cow's Milk*

Author	Subject	Duration of Period, Days	Age, Mo.	Weight, Kg.	Chlorid Intake		Chlorid Output			Chlorid Utilization			Chlorid Retention		
					Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Feces per 24 Hours, Gm.	Urine per 24 Hours, Gm.	Total per 24 Hours, Gm.	Per 24 Hours, Gm.	Per Kg. per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Kg. per 24 Hours. Gm.	Per Cent. of Intake
						Breast Milk									
Freund [5]	1	4	4.5	4.94	0.280	0.056	0.011	0.208	0.219	0.169	0.034	60.21	0.061	0.012	21.75
	2	6	3.0	2.95	0.393	0.136	0.012	0.258	0.270	0.381	0.127	96.94	0.123	0.041	31.04
Tobler L., and Noll, F.: Monatschr. f. Kinderh. **9**: 210, 1910	1	6	2.5	4.04	0.114	0.028	0.0045	0.0921	0.0960	0.1095	0.027	96.07	0.0174	0.0044	15.26
Lindberg, G.: Ztschr. f. Kinderh. **16**: 90, 1917	1	...	2.5	4.285	0.4189	0.098	0.0214	0.2515	0.2729	0.3976	0.093	94.90	0.1460	0.0034	34.86
				4.370	0.4208	0.096	0.0402	0.2342	0.2744	0.3806	0.087	90.45	0.1464	0.0033	34.79
				4.370	0.3053	0.070	0.0264	0.1188	0.1452	0.2789	0.063	91.35	0.1601	0.0036	52.43
				4.370	0.3215	0.073	0.0588	0.1420	0.2008	0.2627	0.060	81.71	0.1208	0.0028	37.56
Hoobler [3]	1	...	...	.....	0.3297	.....	0.0135	0.1776	0.1911	0.3162	.....	95.4	0.1386	.....	42.04
Blauberg [2]	1	6	5	.....	0.3350	.....	0.0231	0.0215	0.0456	0.3119	.....	93.1	0.2894	.....	86.4
Michel, C., and Perrett, M.: Bull. Soc. d. obst. et de gynec. **2**: 98, 1899	...	...	3	4.725	0.4586	0.098	0.0170	0.3284	0.3454	0.4416	0.094	96.3	0.1139	0.024	24.8
Klotz, M.: Jahrb. f. Kinderh. **70**: 1, 1909	...	...	2.5	3.42	0.3696	0.108	0.1210	0.0931	0.2141	0.2485	0.073	67.25	0.1555	0.046	42.05
						Cow's Milk									
Hoobler [3]	...	...	9	....	2.3178	.....	0.042	2.2421	2.2841	2.2758	0.274	98.1	0.0337	0.004	1.4
Blauberg [2]	...	...	...	....	0.2850	.....	0.1170	0.3952	0.5122	0.1680	.....	59.0	—0.2272	.....	.....
Tangle [9]	...	...	3.0	4.51	1.469	0.326	0.046	1.306	1.352	1.422	0.315	96.8	0.117	0.026	7.96
			4.7	5.41	1.148	0.212	0.041	1.006	1.047	1.107	0.205	96.4	0.101	0.019	8.80

The figures of Table 3 are difficult to compare with ours. The range there tabulated, with breast milk, is from 0.0215 gm. to 0.3284 gm. per twenty-four hours. This discrepancy might well be due to the much lower intake, since more than 50 per cent. of these cases had a chlorid intake less than our minimum. In the cases where the intake of sodium chlorid approximates that of our cases the urinary sodium chlorid is also within our range, with the exception of the case reported by Blauberg,[2] where the excretion is exceptionally low and the retention unusually high. Blauberg [2] in his one case with cow's milk had a very low intake and a low excretion. Hoobler [3] reported a very high intake and a correspondingly high excretion. Tangle's [9] cases check quite well with ours.

The Effect of the Change of Milk on the Utilization and Retention of Chlorids.—Since the chlorid is mainly eliminated through the urine, the actual value of the utilization runs parallel to the urinary chlorids. As urinary chlorid depends on intake, the utilization in grams per twenty-four hours is always higher on a diet of cow's milk. With breast milk the utilization varies from 0.2934 gm. to 0.4871 gm. with an average of 0.3847 gm. In the case of cow's milk the corresponding figures are from 1.1456 gm. to 1.7021 gm. with an average of 1.3691 gm. Although the actual quantity of sodium chlorid utilized from the two milks varies so greatly, there is no marked difference in the percentage utilization. The ranges are for breast milk from 72.3 to 98.1, with an average of 87.4 per cent. as against cow's milk from 81.0 to 98.5, with an average of 92.2 per cent. Here again, the work reported in Table 3, with the exception of those cases where the intake was very low, is in fairly close agreement with our figures. Excluding two cases, their figures ran from 0.2485 gm. to 0.4416 gm. with breast milk. Their percentage utilization runs from 60.2 to 96.9.

There were three cases with breast milk and two with cow's milk in which one day during the period showed a negative retention value. However, the average of three-day periods always gave a positive value. There is a much greater variation in retention in different individuals than in utilization. With breast milk the figures range from 0.0019 gm. to 0.2218 gm. per twenty-four hours, with an average of 0.0886 gm. For cow's milk the range is from 0.0704 gm. to 0.3978 gm. with an average of 0.2710 gm. Here again, however, the average percentage values follow each other very closely, that of breast milk being 19.2 per cent. and cow's milk 18.9 per cent. So it seems that the variation in the intake is accompanied by a corresponding variation in utilization and retention in the same direction, resulting in a constant percentage. This is a fact for which it is very difficult to account.

The values for retention reported by other investigators also vary within wide limits. Their figures for breast milk run from 0.0174 gm.

to 0.2894 gm., or from 15.3 to 86.0 per cent. The four cases reported using cow's milk are again hard to compare with ours. Hoobler[3] reported a utilization of 2.2758 gm. per twenty-four hours, or 98.1 per cent. of the intake, and a retention of 0.0337 gm. or 1.4 per cent. Blauberg's[2] case gave unusually low values, utilization of 1.680 gm. per twenty-four hours, or 59.0 per cent. Tangle[9] had an average retention of 0.109 gm., or 8.38 per cent.

Relation of Age to Chlorid Utilization and Retention.—Table 4 shows that although there is no marked difference in the utilization, the actual grams retained in the body varied inversely with age; thus the youngest infant, B. N., at 0.4 months had a retention of 0.3978 gm. per twenty-four hours. The corresponding figure for E. M. at 5.5 months, was 0.0704 gm. The percentage retention varied in the same way. The actual quantity of chlorid utilized showed no consistent relation to age, but the percentage had the same tendency as that for retention. In the case of breast milk there was no relation between age and utilization and retention, as may be seen from Table 5. The tendency toward greater retention of chlorids in the younger infants might possibly be due to the more rapid growth of the younger organism and the consequent need for a larger amount of chlorid. We are unable to account for the variation in results between breast milk and cow's milk.

TABLE 4.—*Relation of Age to Chlorid Metabolism, Cow's Milk*

Name	Age, Months	NaCl Utilization		NaCl Retention		Blood Chlorid Per 100 C.c. of Plasma, Mg.
		Per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Cent. of Intake	
B. N.	0.4	1.2134	98.5	0.3978	32.3	552.9
B. B.	1.3	1.5238	97.2	0.3655	23.3	559.1
B. B.	2.1	1.7021	96.1	0.3018	17.3	540.0
W. O.	3.0	1.1456	88.1	0.2578	19.8	650.0
T. O.	4.3	1.3220	92.1	0.2329	16.2	658.0
E. M.	5.5	1.3077	81.0	0.0704	4.4	748.7

TABLE 5.—*Relation of Age to Chlorid Metabolism, Breast Milk*

Name	Age, Months	NaCl Utilization		NaCl Retention		Blood Chlorid Per 100 C.c. of Plasma, Mg.
		Per 24 Hours, Gm.	Per Cent. of Intake	Per 24 Hours, Gm.	Per Cent. of Intake	
B. N.	1.4	0.3023	89.6	0.0765	22.7	501.3
B. B.	1.6	0.4309	96.2	0.0837	18.7	601.8
W. O.	2.6	0.2934	72.3	0.0853	21.0	615.6
T. O.	3.2	0.3739	98.1	0.0019	0.5	629.3
W. O.	3.3	0.4871	89.3	0.2218	40.7	614.2
E. M.	5.7	0.4204	78.8	0.0626	11.7	804.0

Relation of Blood Chlorid to the Chlorids in Breast Milk and Cow's Milk.—For blood chlorid, Rusznyák's[10] method was followed and the determinations were made on the plasma. Tables 4 and 5 show no relation between the kind of milk fed and the chlorid content of the blood, but of six tests on each milk two had a higher blood chlorid with breast milk and four with cow's milk. The average figure for blood chlorid with breast milk was 627.7 mg. per hundred cubic centimeters of plasma, and that of cow's milk was 618.1 mg. per hundred cubic centimeters of plasma. The time of drawing blood was not controlled in relation to the meals, and so the varying results in several cases may be due to the time factor. Scheer [11] and Dodds and Smith [12] call attention to the fact that blood chlorids are lowered shortly after a meal, due to the gastric secretion of hydrochloric acid.

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[10] Rusznyák, S.: Eine Methode zur Bestimmung der Chloride in kleinen Flüssigkeitsmengen, Biochem. Zeit. **114**:23, 1921.

SUMMARY

1. Change of diet from breast milk to cow's milk was invariably followed by an increase in the chlorid excretion in both feces and urine, and vice versa. The increase is due, at least in part, to the increased chlorid intake in cow's milk. The average intake with cow's milk was 1.4817 gm. per twenty-four hours and with breast milk 0.4441 gm. The average excretion in feces was 0.1128 gm. and 0.0576 gm. respectively, and in urine 1.0988 gm. and 0.3298 gm.

2. The utilization of chlorids runs parallel to the urinary chlorid; with breast milk it is 0.3847 gm. per twenty-four hours and with cow's milk, 1.3691 gm. There is no marked difference in percentage utilization of chlorid intake between the two milks. For breast milk the average utilization was 87.4 per cent. as against 92.2 per cent. for cow's milk.

3. There was great variation in chlorid retention in different individuals. The average retention for breast milk was 0.0886 gm. per twenty-four hours, or 19.2 per cent., and for cow's milk 0.2710 gm. or 18.9 per cent.

4. As age increased there was a decrease in the actual amount of chlorid retained with cow's milk, but no such relation existed with breast milk; neither was there any definite relation between age and percentage retention.

5. Change of milk had no effect on the chlorid content of the blood. On a diet of breast milk the average blood chlorid was 627.7 mg. per hundred cubic centimeters of plasma, and on cow's milk it was 618.1 mg.

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11. Scheer, K.: Untersuchungen über den Chloridgehalt des Serums beim Säugling unter verschiedner Bedingungen, Jahrb. f. Kinderh. **94**:295, 1921.

12. Dodds, E. C., and Smith, K. S.: Variations in the Blood Chlorids in Relation to Meals, J. Physiol. **58**:157 (Dec.) 1923.

THE EFFECT OF FLUID ON THE TEMPERATURE AND BLOOD CONCENTRATION IN THE NEW-BORN WITH FEVER *

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In a previous paper [1] evidence was presented to show that a close relationship exists between fever in the new-born and dehydration. Whereas in afebrile new-born infants the protein concentration of blood serum is fairly constant, usually lying between 6 and 7 per cent., in the new-born with fever the serum proteins are generally above 7.5 per cent. and often over 9 per cent., indicating a marked diminution in the plasma water.

In the experiments reported in this paper the effect of fluid therapy on the temperature and blood concentration of the new-born with fever was studied. Approximately 35 c.c. of fluid per kilogram of body weight (a total of from 100 to 150 c.c.), warmed above the temperature of the baby, were given and the temperature and blood concentration determined repeatedly before and after the fluid administration. The fluid was given in various ways—orally (gavage), hypodermically and intraperitoneally. The gavage method for introducing fluid into the stomach was used so that a large amount of fluid could be given quickly. It is probable that similar results would be obtained if the fluids were given by mouth in the usual manner. Tap water, saline and glucose solution were the fluids used. The babies were kept well covered during the experiments to avoid a fall in temperature due to cooling of the body surface. Benedict and Talbot [2] have emphasized the importance of this factor in reducing the temperature of the new-born with fever. The same thermometer was used throughout each experiment.

Variations in the blood concentration were estimated from changes in the protein concentration of serum and also, in most instances, from changes in the red cell count. The technic used for determining the serum protein concentration was similar to that described in previous

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* Received for publication, March 13, 1924.

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[1] Bakwin, H.: Dehydration Fever in the New-Born, II., Am. J. Dis. Child. **24**:508 (Dec.) 1922.

[2] Benedict, F. G., and Talbot, F.: Carnegie Institute Publications, No. 233, 1915.

papers.[3] The pipets and counting chamber used for the red cell counts were standardized by the Bureau of Standards. Dilutions were made with Hayem's solution and the mixtures shaken in a mechanical shaker.

The effect of water by mouth on the temperature and blood concentration of infants, from 2 to 15 months of age, with fever due to various infections was studied as a control group.

RESULTS

The Effect of Fluid by Mouth on the Temperature and Blood Concentration of New-Born Infants with Fever.—When warm water was given by gavage in the proportion of 30 to 40 c.c. per kilogram of body weight, a prompt fall in temperature and blood concentration followed with great regularity (fifteen out of sixteen cases studied). The temperature usually reached normal within an hour. The drop in serum protein concentration ordinarily amounted to about 1 per cent. of protein, representing an increase of approximately 12 per cent. in

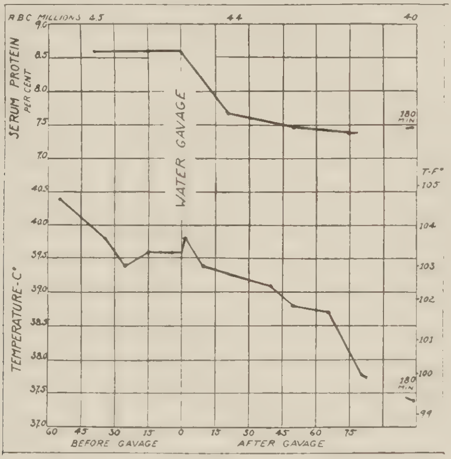

Chart 1.—Water gavage; drop in temperature and blood concentration in a new-born with fever.

Case 5 (Chart 1).—The baby, a boy, healthy at birth, developed fever on the sixth day after a weight loss of 510 gm. The mouth and tongue were dry and the skin loose and inelastic. The stools were frequent, green and watery. The serum proteins were 8.61 per cent., indicating a marked diminution in the plasma water. Following a gavage of 100 c.c. of warm water the temperature fell, reaching the normal level in two hours and remained normal during the rest of the baby's stay in the hospital. Coincident with the drop in temperature there was a fall in the serum protein concentration from 8.61 to 7.37 per cent. The red cells fell from 4,500,000 per cubic millimeter to 3,960,000.

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[3] Bakwin, H.: Dehydration in the New-Born, I., Am. J. Dis. Child. **24:**497 (Dec.) 1922.

the plasma water. The fall in the red cell count was more marked than would be expected from the drop in the serum protein concentration and represented, in most instances an increase of about 15 per cent. in the whole blood water. The results in four typical cases are shown in Charts 1 to 4.

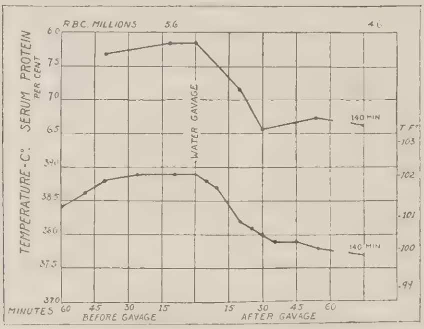

Chart 2.—Water gavage; prompt drop in temperature and blood concentration in a new-born with fever.

Case 6 (Chart 2).—The baby, a girl, vigorous at birth, developed fever on the second day of life after a loss of 330 gm. Following a water gavage of 100 c.c. the temperature fell to normal in an hour. The serum proteins dropped from 7.84 per cent. to 6.74 and the red cells from 5,630,000 to 4,580,000 per cubic millimeter.

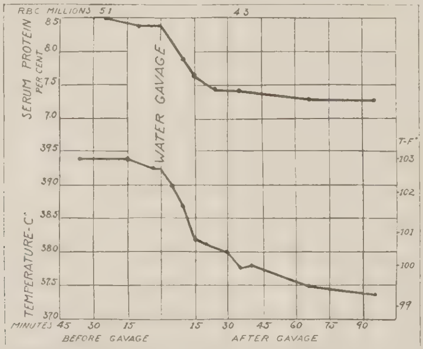

Chart 3.—Water gavage; prompt drop in temperature and blood concentration in a new-born with fever.

Case 7 (Chart 3).—The baby, a girl, developed fever on the third day of life after a weight loss of 320 gm. The mucous membranes of the mouth were dry and red and the skin was loose and inelastic. The baby cried continuously and took the breast eagerly. The serum protein concentration was 8.55 per cent., indicating a marked decrease in the plasma water. The temperature fell to normal within an hour after a gavage of 110 c.c. of warm water. There was a simultaneous drop in the serum proteins from 8.55 to 7.31 per cent., and in the red cell count from 5,080,000 per cubic millimeter to 4,300,000. There was a secondary rise in temperature on the fifth day associated with a loss in weight and an increase in the serum protein concentration to 8.13 per cent. The temperature fell to normal within twenty-four hours after the free administration of water by mouth. There was no further rise in temperature.

The one patient in whom the water gavage failed to reduce the temperature was an infant with severe dehydration and a serum protein concentration of 10.17 per cent. Estimations of the serum proteins were not made after the fluid was given.

The results following the administration of a 5 per cent. glucose solution by gavage were similar to those obtained with water. With saline by mouth there was a tendency to diarrhea and these experiments were consequently discontinued. In one baby, due to an error, a 10 per cent. glucose solution was given instead of a 5 per cent. solution. A profuse, watery diarrhea, similar to that following the administration of a hypertonic salt solution, occurred. The stools, after the first few had been passed, contained no solid material and reduced Benedict's solution strongly. A rise in temperature accompanied the loss of fluid through the diarrhea.

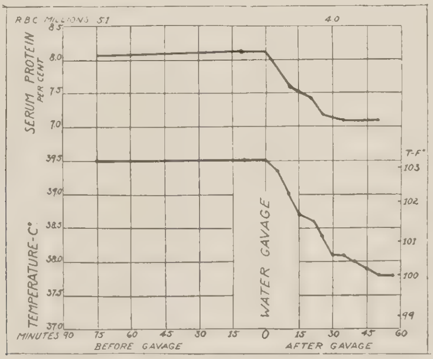

Chart 4.—Water gavage; prompt drop in temperature and blood concentration in a new-born with fever.

Case 8 (Chart 4).—The baby, a girl, developed fever on the third day of life after a weight loss of 420 gm. The skin was dry and inelastic, the mucous membranes of the mouth red and dry and the cord slightly moist. The baby cried incessantly and took the breast eagerly.

The temperature fell to normal within an hour after water gavage (135 c.c.) and remained there until the baby's discharge from the hospital on the twelfth day. Coincident with the drop in temperature there was a fall in the serum protein concentration from 8.06 to 7.09 per cent., and in the red cell count from 5,070,000 per cubic millimeter to 4,030,000.

The Effect of Fluid by Hypodermoclysis and Intraperitoneal Injection on the Temperature and Blood Concentration of the New-born with Fever.—When fluid was given hypodermically or intraperitoneally in amounts varying from 35 to 60 c.c. per kilogram of body weight the effect on the temperature and blood concentration was neither so marked nor so prompt as after water gavage, and occurred much less regularly. Usually a gradual drop of temperature from 0.5 to 1 degree C. in two hours occurred. The drop in the serum

Table 1.—*Saline by Hypodermoclysis Without Any Effect on the Temperature and Blood Concentration in a New-Born with Fever*

Time, a. m.	Temperature		Serum Protein, per Cent.	Red Cells, per Cu. Mm.
	Centigrade	Fahrenheit		
9:00	38.7	101.6	....	....
10:00	39.3	102.8	....	....
10:30	39.4	103.0	8.13	4,180,000
10:45	39.5	103.2	8.30	....
11:15	39.9	103.8	....	....
11:25–11:45 hypodermoclysis, 125 c.c. saline				
11:50	39.7	103.5	....	....
12:00	39.7	103.5	7.78	....
p. m.				
12:15	39.8	103.7	7.78	4,180,000
12:40	39.8	103.7	....	....
1:10	39.8	103.7	7.84	....
1:30	39.5	103.2	7.84	....
2:00	39.5	103.2	....	....
3:00	40.0	104.0	....	....
3:30	40.0	104.0	7.84	....
3:30–4:00 colon irrigation				
4:25	39.4	103.0	7.61	....
4:55	39.3	102.8	7.73	....

Table 2.—*Saline by Hypodermoclysis with an Immediate Fall in Temperature and Blood Concentration Followed by a Secondary Rise in a New-Born with Fever*

Time, p. m.	Temperature		Serum Protein, per Cent.
	Centigrade	Fahrenheit	
3:00	39.3	102.8	7.55
3:10	39.3	102.8	7.55
3:25	39.2	102.6	....
3:45	39.3	102.8	....
4:25	39.0	102.2	8.02
4:40–4:50, hypodermoclysis, 150 saline			
5:00	38.6	101.4	....
5:10	38.4	101.1	7.73
5:20	38.2	100.8	....
5:40	38.1	100.6	7.55
5:50	37.9	100.2	....
6:30	38.1	100.6	7.37
7:45	39.2	102.6	7.55
9:05	39.2	102.6	....
9:10	39.4	103.0	7.96
9:40	39.3	102.8	....
10:15	39.5	103.2	7.78

Table 3.—*Saline by Intraperitoneal Injection Followed by a Slight Transitory Drop in Temperature and Blood Concentration in a New-Born with Fever*

Time, a. m.	Temperature		Serum Protein, per Cent.
	Centigrade	Fahrenheit	
10:00	38.9	102.0	7.76
10:10	38.7	101.6	....
10:25	39.0	102.2	7.95
10:30	39.0	102.2	....
10:45	38.8	101.8	7.61
11:00–11:15, intraperitoneal injection 150 c.c. saline			
11:20	38.7	101.6	7.67
11:25	38.1	100.4	....
11:30	38.6	101.4	....
11:35	38.3	101.0	7.61
12:00	38.5	101.2	7.55
p. m.			
12:15	38.6	101.4	....
12:25	38.6	101.4	7.61
12:55	38.6	101.4	....
1:35	38.4	101.0	7.96

protein concentration rarely amounted to over 0.5 per cent. of protein. In only three of the sixteen babies studied after fluid was given by these routes did the temperature reach normal during the period of observation, which was usually about two hours after the fluid was given. The results in four cases are shown in Tables 1 to 4.

TABLE 4.—*Saline by Intraperitoneal Injection, with a Gradual Fall in Temperature and Blood Concentration in a New-Born with Fever*

Time, a. m.	Temperature		Serum Protein, per Cent.
	Centigrade	Fahrenheit	
10:00	39.7	103.4	7.75
10:30	39.7	103.4	7.61
10:30–10:45, intraperitoneal injection 150 c.c. saline			
10:50	39.4	103.0	7.96
10:55	39.3	102.8	7.61
11:10	39.0	102.2	....
11:15	38.8	101.8	....
11:40	38.6	101.4	7.43
12:00	38.3	101.0	7.55
p. m.			
12:30	38.7	101.6	....
1:00	38.7	101.6	7.49
1:45	38.8	101.8	....

TABLE 5.—*The Effect of Water by Gavage on the Temperature and Blood Concentration of Infants with Fever Due to Various Infections*

Case	Age, Mo.	Weight, Kg.	Diagnosis	Amount of Fluid Given, C.c.	Temperature				Serum Protein, per Cent.		Time Between the Beginning of the Experiment and the Maximum Drop in Temperature
					At the Beginning of the Experiment		At the Time of the Maximum Drop		At the Beginning of the Experiment	At the Time of the Maximum Drop in Temperature	
					F.	C.	F.	C.			
1	9	4.15	Otitis media	210	102.2	39.0	104.2	40.1	7.17	....	2 hrs.
2	10	5.81	Acute bronchopneumonia	150	102.2	39.0	100.8	38.1	8.83	....	2 hrs.
3	15	4.90	Acute bronchopneumonia	210	102.0	38.9	101.0	38.2	7.69	....	2 hrs.
4	3	3.38	Otitis media	150	102.0	38.9	102.8	39.4	5.39	....	2 hrs.
5	10	7.84	Nasopharyngitis	240	102.0	38.9	101.6	38.7	....	....	1½ hrs.
6	4	3.75	Miliary tuberculosis	210	102.0	38.9	101.4	38.6	5.81	5.75	1 hr.
7	8	5.63	Acute bronchopneumonia	180	100.8	38.1	100.4	38.0	7.50	7.09	1 hr.
8	2	3.92	Nasopharyngitis	150	100.8	38.1	100.4	38.0	6.91	6.51	2 hrs.
9	4	3.68	Miliary tuberculosis	180	104.4	40.2	101.0	38.2	6.11	5.87	2 hrs.
10	7	3.83	Nasopharyngitis	150	101.4	38.6	99.6	37.6	5.99	5.99	1 hr.
11	9	6.36	Miliary tuberculosis	225	102.4	39.2	101.6	38.7	7.20	6.91	1½ hrs.

The Effect of Fluid by Mouth on the Temperature and Blood Concentration of Infants with Fever Due to Various Infections.—Water was given by gavage to eleven infants with fever due to various infections. The results are shown in Table 5. In most instances there was a slight fall in the temperature amounting to less than 1 degree C.

In one infant with nasopharyngitis and with a temperature of 38.1 C. (101.4 F.) the temperature dropped to 37.6 C. (99.6 F.) in one hour. The plasma dilution following the water gavage in these older infants with fever was not so marked as in new-born infants with fever.

COMMENT

These results emphasize two points of interest. First, the striking parallelism between the effect of fluid on the blood concentration and on the temperature in the new-born with fever offers strong evidence in favor of the view that this particular type of fever is due to dehydration. A second point of interest is the greater efficacy of the oral over the subcutaneous or intraperitoneal routes in reducing the concentration of the blood and lowering the temperature in the new-born with dehydration. When the fluid is given by mouth it enters the blood promptly, as is indicated by a fall in the serum protein concentration and in the red cell count. When the fluid is given hypodermically or intraperitoneally the fall in blood concentration is neither so marked nor so prompt as after gavage. Apparently a process exists whereby fluid given by mouth is promptly absorbed into the blood and tissues. Fluid given into the subcutaneous tissues or the peritoneal cavity enters the blood much more slowly and to a much less extent.

Similar results were obtained by one of us (B.) in older infants dehydrated as a result of severe diarrhea. During the summer of 1921 a series of these infants was treated with fluid by mouth. Water or 5 per cent. glucose solution was dripped into the stomach at a slow rate by means of a tube inserted into the stomach through the nose. A fine catheter (No. 8 French), well lubricated, was used and the fluid administration continued for several hours. A drop in blood concentration, an improvement in the skin turgor and an increase in the urine flow followed when fluid was given in this manner. When the fluid was given hypodermically or intraperitoneally the increase in plasma water was slight or entirely absent and there was usually no effect on the urinary flow. An improvement in the skin turgor in the neighborhood of the fluid injection was frequently observed.

It is of interest to note in this connection that Robertson and Bock [4] found that, in adults with post-hemorrhagic anemia, fluid by mouth was second only to blood transfusion in the rapidity with which it increased the blood volume.

SUMMARY AND CONCLUSIONS

1. The effect of fluid on the temperature and blood concentration of the new-born with fever was studied.

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[4] Robertson, O. H., and Bock, A. V.: The Use of Forced Fluids by the Alimentary Tract in the Restoration of Blood Volume After Hemorrhage, J. Exp. Med. **29**:155 (Feb.) 1919.

2. When fluid was given by mouth in the proportion of from 30 to 40 c.c. per kilogram of body weight a prompt fall in the temperature and blood concentration followed with great regularity. The temperature usually reached normal within from 30 to 90 minutes.

3. When the fluid was given hypodermically or intraperitoneally, the effect on the temperature and blood concentration was neither so marked nor so regular as after water by mouth.

4. Water by mouth, in amounts similar to those used in the newborn with fever, has practically no effect on the temperature of infants with fever due to various infections.

5. In a group of older infants, dehydrated as a result of severe diarrhea, fluid by mouth was much more effective in reducing the concentration of the blood than fluid given by hypodermoclysis or intraperitoneal injection.

REPORT OF CASES

CASE 1 (Table 1).—The baby, a girl, was delivered normally at term and weighed 3.21 kg. On the third day, after a loss of weight of 300 gm., she developed fever. The serum protein concentration was 8.30 per cent., indicating a marked diminution in plasma water. A subcutaneous injection of saline was given. There was no change in the temperature or red cell count. The serum proteins fell slightly. The fever persisted for twenty-four hours, after which time it fell to normal and remained there until the baby's discharge from the hospital, which occurred on the eleventh day.

CASE 2 (Table 2).—The baby, a boy, was vigorous at birth and weighed 4.50 kg. The protein concentration of the placental serum was 7.61 per cent., indicating a slight diminution in the plasma water. He developed fever on the second day after a loss of weight of 450 gm. He was somnolent and limp and cried very little. The skin was dry and inelastic, the mucous membranes of the mouth dry and red. The serum proteins had risen to 8.02 per cent. A subcutaneous injection of saline was given. A slight fall in temperature and blood concentration occurred during the ninety minutes after the hypodermoclysis but both rose again quickly. The temperature remained elevated for three days, after which it dropped to normal and remained there until the baby's discharge from the hospital.

CASE 3 (Table 3).—The baby, a boy, was delivered normally and weighed 3.84 kg. He developed fever on the second day after a loss of 90 gm. The serum proteins were 7.96 per cent. The skin was dry and inelastic, the mouth and lips dry. An intraperitoneal saline injection was given. There was a slight fall in temperature and blood concentration during the forty-five minutes after the injection followed by a secondary rise.

CASE 4 (Table 4).—The baby, a girl, developed fever on the second day after birth, after a loss of 330 gm. The next day she had lost an additional 240 gm. and the temperature rose to 40 C. (104 F.). She was somnolent and limp and appeared ill. The skin was moderately inelastic, the mouth dry and red. She took the breast eagerly. The serum proteins were 7.78 per cent. An intraperitoneal injection of saline was given. There was a slight drop in temperature and serum concentration. Fever persisted for another day after which the baby was afebrile except for a slight rise in temperature, associated with a loss in weight and an increase in the serum protein concentration, on the eleventh day.

TUBERCULOUS PULMONARY CAVITIES IN INFANCY *

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Tuberculous pulmonary cavities in infancy would seem at first glance to be a very rare condition. A review of the available literature demonstrated, as it so often has done in the past, that this occurrence, while indeed uncommon, is not at all rare. The French literature, especially, supplies numerous instances of cavity formation following tuberculous infection. Our own literature is surprisingly meager on this subject. The purpose of this paper is the presentation in detail of a case showing several unusual and interesting features. A review of available case reports is submitted.

REVIEW OF LITERATURE

In 1888, Leroux,[1] in a study of 219 infants from birth to 2 years of age, was able to demonstrate cavities in fifty-seven cases. Twelve cases were under 6 months of age and five cases were under 3 months.

In 1897, Babeau [2] reported a case of cavity formation in an infant 10 months old. Later in the same year, Ausset [6] reported a cavity in an infant 14 months old.

Comby,[3] in 1898, found seven cases of cavity formation in twenty infants dying of tuberculosis.

Kuss [4] and d'Aviragnet [5] in extensive Paris theses published during the same year, summarized all the available French literature. They found that cavities occurred with surprising frequency. During the first year of life one out of every five patients dying of pulmonary tuberculosis showed evidence of cavity formation.

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* Received for publication, Dec. 20, 1923.

* From the department of pediatrics, University of Minnesota.

* Read before the medical staff of the Lymanhurst School for Tuberculosis Children, May 22, 1923.

[1] Leroux: La tuberculose du premier âge. Études expérimentales et cliniques sur la tuberculose, Paris, 1888, p. 2.

[2] Babeau, Joseph: Tuberculose généralise caverne pulmonaire chez une enfant de dix mois, J. de clin. et de thérap. inf., Paris, **5**:483-487, 1897.

[3] Comby: Tuberculose pulmonaire chez l'enfant, Arch. d. mal. des enfants, 1898.

[4] Kuss: Tuberculose cavitaire en un enfant, Thèse de Paris, 1898.

[5] D'Aviragnet: Tuberculose cavitaire chez un enfant, Thèse de Paris, 1898.

In 1899, Ausset[6] reported a tuberculous cavity in an infant aged 11 months. During the same year, Griffon[7] reported a cavity in an infant 6 months old.

Rabot and Varay,[8] in 1902, described the necropsy on an infant 5 months old. The right lung showed two cavities, the size of a hazel nut and a pea, respectively. The left lung showed a cavity the size of a large pea. Mayound,[9] at the same time, reported a cavity in an infant 3 months old.

In 1903, Hautant[10] cited a case in an infant aged 9 months. In the same year, Mairesse,[11] in his Paris thesis, reviewed thirty-five cases in infants ranging from 2 months to 2 years of age. He concluded that cavitation in early infancy was rare and they were exceptional before the first year. He thought they were due to a rapid "melting of a caseous pneumonia."

In 1905, Delarde[12] reported the case of a 10 months infant.

Lortat and Vitry,[13] in 1905, demonstrated a cavity the size of a grain of hempseed in an infant 2 months old.

Geipel,[14] in 1906, justly emphasized a critical review of the reported cases. In thirty-four cases of tuberculosis in infancy, he found thirteen cases of cavity. Later, in 1906, Koch-Elberfeld[15] published a case of a cavity formation in a child aged 5 months.

About the same time, in 1906, L'Homme,[16] in a thorough research, reviewed thirty-nine cases collected from the literature (including three of his own). His patients varied in age from birth to 24 months. He

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6. Ausset, M.: Tuberculose cavitaire, en un enfant de onze mois, Rev. mens. d. mal. d'l'enf. **17**:332, 1899; Centr. Med. Soc. du Nord, May 12, 1899.

7. Griffon, M. V.: Phlébite oblitérant de la vein cave inférieure dans un cas de tuberculose cavitaire de la premier enfance, Rev. Mens. d. mal. de l'enf. **17**:30, 1899.

8. Rabot, and Varay, F.: Tuberculose pulmonaire ulcéreuse (cavernes) chez un enfant de cinq mois, méningite tuberculeuse (forme hémiplégique), Rev. Mens. de mal. de l'enf. **20**:246-254, 1902.

9. Mayound: Caverne pulmonaire chez un nourrisson, Lyon Méd., **98**:21-22, 1902.

10. Hautant, M. A.: Tuberculose pulmonaire avec grande caverne, chez un enfant de neuf mois, Tubercul. Inf., Paris **6**:83-87, 1903-1906.

11. Mairesse, Marcel: Des cavernes pulmonaires tuberculeuse dans le premier âge, Paris Thèses, 1903-1904.

12. Delarde, M.: Caverne pulmonaire chez un enfant de dix mois, Echo méd. du nord, Lille **9**:606, 1905.

13. Lortat, Jacob, and Vitry, G.: Caverne pulmonaire chez un nourrisson, Cong. Interat. de la tuberc., Par. **2**:350-355, 1905.

14. Geipel, P.: Ueber Sauglings-tuberkulose, Ztschr. f. Hyg. u. Infectionsfrankh., Bd. **53**:51-58, 1906.

15. Koch-Elberfeld, Max: Kavernose Lungenphisis bei einem fünf Monate alten Kind, Verhandl. d. deutsch. path. Gesellsch. **10**:262-264, 1906.

16. L'Homme, Henri: Contribution a l'étude de la tuberculose chez le nourrisson dans la premier enfance, Paris Thèses, 1905-1906.

quoted Huguenin[17] as reporting a case of cavity formation in a newborn infant. He also cited Berti's[18] case of lung cavity in an infant 9 days old. From his studies he concluded that cavity formation was uncommon but not rare and that its clinical diagnosis was exceedingly difficult. He thought that the prognosis was not always fatal, but that it usually was fatal.

Monges,[19] in 1907, published a report showing cavity formation in an infant 4½ months old. Sauvan[20] reported, in the same year, a tuberculous cavity in a 13 months old infant.

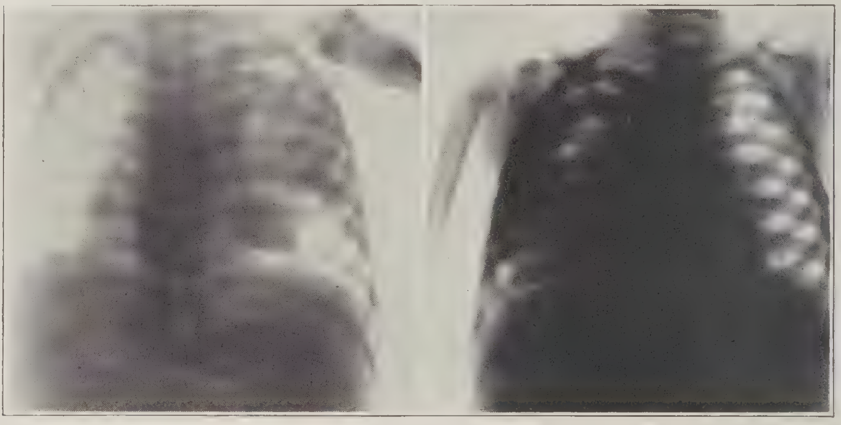

Fig. 1.—Left: Marked density along the hilum and root of right lung and irregular density of its entire upper lobe, a suggestion of a large anular shadow between first and third ribs near hilum, giving the impression of a resolving lobar or bronchopneumonia. (The roentgenogram is reversed.) Right: Right lung field showing irregular density throughout, except in apex and base; a large annular shadow within this dense area in second and third interspaces near hilum, which simulates a cavity. The general appearance of the lungs has not changed materially, except for a greater prominence of the annular shadow. The impression given was probable of a pulmonary tuberculosis with irregular consolidation and a large cavity in the right upper lobe.

White and Carpenter,[21] in 1909, in an excellent presentation of the subject, reported six cases of cavity formation, occurring in colored infants between 5 and 15 months old. In every instance the diagnosis was made at necropsy.

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17. Huguenin: Tuberculose des nouveau-né et tuberculose congénital, Gaz. d. Hôp. **61**:785, 1888.

18. Berti, G.: Interus ala possibilite di processi tisiogeni congeniti, Bol. del. scien. med. **10**:29, 1882.

19. Monges, M. J.: Cavernes tuberculeus chez un enfant de quatre mois et demi, Marseille méd. **44**:153, 1907.

20. Sauvan, M.: Caverne tuberculouse chez un enfant de treizième mois, Marseille méd. **44**:343, 1907.

21. White, C. Y.; and Carpenter, H. C.: Tuberculose Pulmonary Cavities in Infants, Am. J. M. Sc. **138**:79-92 (July) 1909.

During the same year, Gaujoux and Brunel[22] collected forty-one cases from the French literature, and in a very thorough and careful study presented their results. There were only twenty-four cases showing cavitation up to 2 years of age. They emphasized the difficulties of clinical diagnosis and the importance of a critical study of cases reported as showing cavitation.

Chalier,[23] also in 1909, presented a patient 1½ years old.

In 1910, Collet and Delachanal[24] cited the case of a 3 months old infant in which they found one cavity at the apex of the right lung, and another in the lower lobe. They thought that cavities in babies were formed by a rapid caseation necrosis of lung tissue and not by a fibrocaseous process as in the adult.

Buddy,[25] in 1911, reported a baby girl, 3 months old, showing an abscess cavity.

Ribadeau-Dumas,[26] in 1913, laid emphasis on the value of the roentgen ray in the diagnosis of tuberculous cavities. Clinical findings were unreliable because of the small size of the lesions. He found that they varied from that of a nut to that of a pea. He thought that it was due to this factor that the condition is found so rarely.

In 1914, Wollstein and Bartlett,[27] in an extensive study of tuberculous lesions in infants and young children based on necropsy examinations, drew some interesting conclusions. In 178 necropsies on tuberculous children, pulmonary cavitation was present in forty-three. The right lung was more frequently involved than the left. Twenty patients were less than 1 year old and the youngest was 3¾ months. They found that "cheesy degeneration in the lungs of these young children takes place and extends rapidly."

In 1915, Randolph[28] reported a case of cavitation of the lung in an infant dying in the seventh month.

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22. Gaujoux, E., et Brunel: La tuberculose pulmonaire caverneuse chez L'enfant, Ann. de méd. et chir. inf. **13**:397-401, 443, 472, 1909.

23. Chalier, M. J.: Tuberculose cavitaire de la base, greffec sur un ancien, Foyer de bronchopneumonie, chez un enfant de un an et demi, Lyon méd. **113**: 743-745, 1909.

24. Collet and Delachanal: Cavernes tuberculeuse chez un nourrisson de trois mois, Lyon Méd. **115**:317-321, 1910.

25. Buddy, E. P.: Report of a Case of Pulmonary Tuberculosis with Cavity Formation in an Infant Aged Three Months, J. Missouri M. A. **8**:359-360, 1911-1912.

26. Ribadeau-Dumas: Tuberculose cavitaire du premier âge, Bull. et. mém. Soc. méd. d. hôp. de Paris **36**:936-942, 1913.

27. Wollstein, Martha, and Bartlett, F. H.: A Study of Tuberculous Lesions in Infants and Young Children, Based on Postmortem Examinations, Am. J. Dis. Child. **8**:362-377 (Nov.) 1914.

28. Randolph, B. M.: Case of Cavitation of Lung in an Infant Dying in the Seventh Month, Washington M. Ann. **13**:149-150, 1914-1915.

Bergmann,[29] in the same year, published a case report of an infant 82 days old.

Canelli,[30] in 1919, found twenty-five cases of cavernous tuberculosis in 175 patients dead of pulmonary infection.

In the second 6 months of life true cavities were seen in four instances.

Ribadeau-Dumas is quoted as saying that he found cavernous pulmonary tuberculosis in 32.4 per cent. of cases during the first 2 years of life.

In 1921, Schott[31] reported multiple cavities in an infant aged 9 months. The cavities were of the honeycomb type, of good size, sharply limited and with smooth walls.

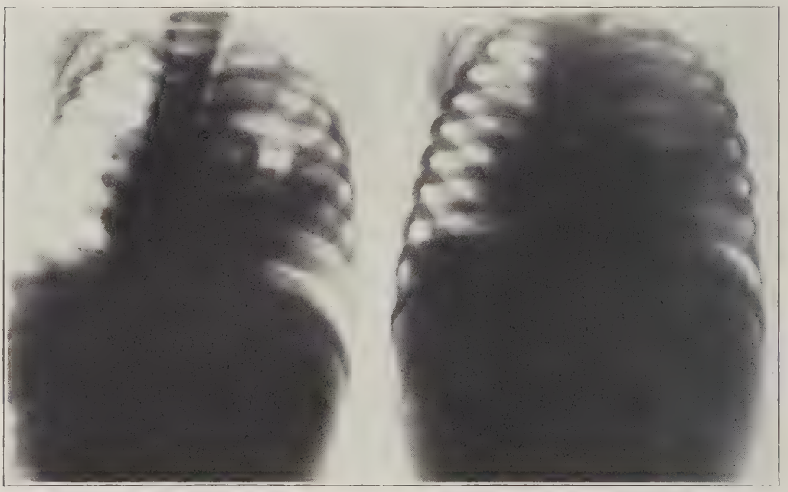

Fig. 2.—Left: The appearance of the right lung is about the same as in Figure 1. The cavity now appears to be well defined. Right: The appearance of the chest is about the same as Figure 1. The cavity is apparently the same size. The consolidation appears to be more homogeneous in density and has extended into the periphery.

REPORT OF CASE

History.—A boy, colored, aged 2 years, was admitted to hospital, Dec. 6, 1922, with the complaint of shortness of breath, fever, loss of appetite, and cough of one month's duration.

Past History.—The patient was born at full term after a normal delivery, and weighed 8 pounds (3,628 gm.) at birth, he was breast fed for five months.

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[29] Bergmann, H.: Cavernöse Lungentuberkulose beim Säugling, Berl. klin. Wchnschr. **52**:577-579, 1915.

[30] Canelli, Adolfo: Contributo alla conoscenza delle localizzazioni della tubercolosinelli primae eta, Riv. di. clin., pediat., Firenze, **17**:523, 1919.

[31] Schott, A.: Ueber eine eigenartige tuberkulose Wabenlungen in Säuglingsalter, Beitr. z. Klin. d. Tuberk. **48**:112 (June 10) 1921.

He had no diseases, except a severe attack of pertussis in July. There was no history of tuberculosis in the family or no exposure to tuberculosis.

Physical Examination.—On admission the temperature was 104; the pulse 120. The patient was well developed, fairly well nourished, irritable and restless. The eyes, ears, nose and throat were negative. The heart tones were rapid but regular. The lungs had an impaired resonance over the entire right side posteriorly with numerous moist râles heard throughout this area. Moist râles were also present in the left lower lobe. Tubular breathing was present over the right upper lobe posteriorly. The liver and spleen were palpable 4 cm. below the costal margin.

Laboratory Findings.—Urine, amber, acid, specific gravity, quantity not sufficient; albumin, negative; pus cells, 2 per high power field; blood, hemoglobin 70 per cent.; red blood counts, 4,400,000, leukocytes, 15,750; polymorphonuclears, 89 per cent.; lymphocytes, 11 per cent.; Wassermann test, negative repeatedly. the Pirquet and Mantaux tests were positive; no tubercle bacilli were demonstrated in the feces.

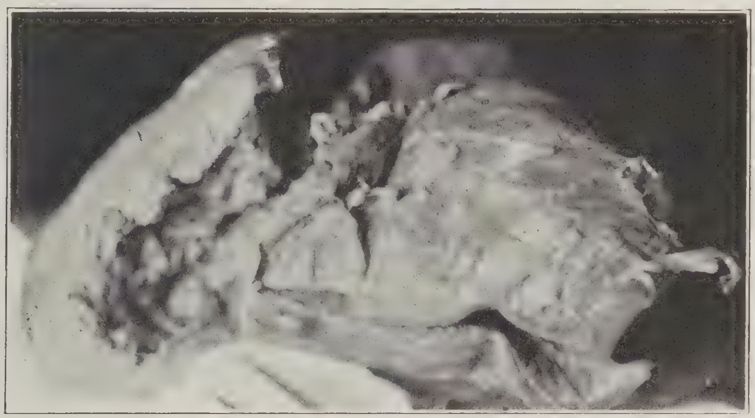

Fig. 3.—Right lung, weight 310 gm., showing thickened adherent pleura, minute miliary nodules and a large cavity containing a large amount of pus. The cavity, located at the junction of the medial and post parts of the upper lobe, measured 5 by 4.5 cm.

On December 14, the patient showed no charge in condition. He had a temperature varying from 99 to 103 daily. The physical findings in the chest increased and were apparently limited to the right side. December 30, the chest plates became more suggestive of possible cavity formation. There was no change in the physical findings. Jan. 10, 1922, the condition remained the same. February 4, the patient lost weight in the last week, and was failing very rapidly. There was no evidence of meningitic involvement. The patient died on February 5, at 8:50 a. m.

Necropsy.—This was limited to the chest. We are indebted to Dr. J. Wendell Gullikson for the pathologic report.

The body was that of a well developed, but emaciated colored child, measuring 85 cm. in length. There was an abscess in the left ischiorectal fossa.

The pleural cavities were obliterated by fibrinous adhesions. The pericardial cavity contained about 25 c.c. of clear straw colored fluid. The liver extended 8 cm. below the root of the xiphoid and 8 cm. below the costal margin in the midclavicular line, almost down to the anterior superior spine of the ilium.

The heart weighed 16 gm. The muscle was slightly pale; otherwise the heart was normal. The root of the aorta was normal. The left lung weighed 150 gm. It was tightly adherent to the thoracic wall by fibrinous and fibrous adhesions. Crepitation was markedly reduced. There was a whitish nodule under the pleura measuring 2 by 1 cm. This nodule was located near the lower part of the lateral surface of the lower lobe. On section this nodule appeared to be quite firm. Section of the remainder of the lower lobe showed an increased amount of frothy fluid with some pus expressible in some dense areas.

The right lung weighed 310 gm. It was firmly bound down with fibrinous adhesions anteriorly and laterally and by fibrinous adhesions posteriorly. Manipulation of the right lung in removing it ruptured a cavity and much pus escaped. The cavity was located at the junction of the medial and posterior parts of the upper lobe and measured 4 by 5 cm. There was a small cavity measuring 1.5 cm. in diameter near the apex. The lower part of the lower lobe was infiltrated with smaller whitish nodules which on section were harder than the normal lung tissue. Pus was also expressible from the bronchi.

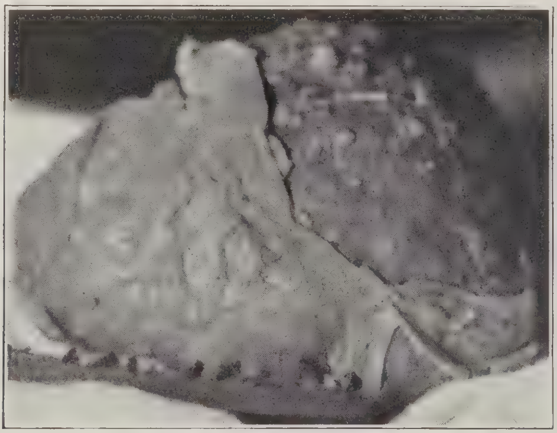

Fig. 4.—Spleen, weight 130 gm. The capsule was tense and literally covered with whitish nodules, varying in size from a pin point to 5 mm. in diameter.

The spleen weighed 130 gm. Its capsule was tense and was literally covered with whitish nodules which appeared to be in the substance of the organ, and which varied in size from a pin point to 5 mm. in diameter. The left kidney weighed 60 gm. The vessels on the surface were slightly congested. Section showed some pallor of the pulp. Section of the liver showed a few small whitish nodules with a yellowish tinge. The mesenteric lymph nodes were greatly enlarged and some of them measured up to 1.5 cm. in length. They were very hard to the touch. Some showed evidence of caseation. The peribronchial lymph nodes were also greatly enlarged and showed some caseation on section.

Diagnosis.—The final diagnosis was: (1) Pulmonary tuberculosis with cavities in the right lung; (2) miliary tuberculosis of spleen and liver; (3) tuberculous adenitis; (4) slight bronchopneumonia; (5) fibrinous and fibrous pleuritis.

COMMENT

A review of the literature on cavity formation during the first 2 years of life is unsatisfactory. In many instances, particularly in the French literature, the age of the patient is not given, and only a very cursory description of the findings are submitted.

The frequency of occurrence of pulmonary cavitation is uncertain. Apparently the results are dependent on the observer and on the locality. While some men find cavities very common, others still consider them rare. Garrod, Batten and Thursfield,[32] in speaking of tuberculosis in early life, say, "Well marked, cavernous signs are seldom present and consequently it is sometimes said that cavities are rare in early life. This, however, is incorrect; they are frequently seen on the necropsy table."

Schlossman [33] holds the same opinion. On the other hand, Smith,[34] in a recent paper, reports statistics on 200 consecutive necropsies from the Infants Hospital of Boston, showing an incidence of 20 per cent. tuberculous. The distribution of the lesions is discussed but apparently no cavity formation was found.

Morse [35] recently made the following statement: "In my experience, cavities in the lungs in childhood are very seldom due to tuberculosis, because children, as a rule, die before cavities have formed."

Our pediatric textbooks dismiss the subject with the statement that cavities may occur at any age.

The subject is one of considerable theoretic and some practical interest. More case reports and thorough discussions are desirable.

The case we report is of interest because the clinical findings suggesting cavity formation were confirmed by our roentgen-ray studies. A diagnosis of pulmonary cavity of tuberculous origin was made during the life of the infant. This is the first reported case, so far as we know, in which the diagnosis made prior to necropsy was confirmed later. The prolonged period of observation gave an excellent opportunity for careful clinical and roentgen-ray study, showing the progressive formation of the cavity.

CONCLUSIONS

1. A review of available literature concerning pulmonary cavitation of tuberculous origin in infants up to 2 years of age, with special regard to incidence, is submitted.

2. A case of tuberculous pulmonary cavity in an infant 2 years of age is confirmed at necropsy.

3. Tuberculous cavities in infants are the result of caseous pneumonia, and not of chronic ulcerative tuberculosis as in adults.

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[32] Garrod, A. E.; Batten, F. E., and Thursfield: Diseases of Children, Tuberculous Cavities, London, 1913, p. 1116.

[33] Schlossman: Ueber Tuberculose, Berl. klin. Wchnschr., Oct. 6, 1902, p. 951.

[34] Smith, L. W.: Tuberculosis in Infancy and Childhood, Am. Rev. Tuberc. **6**:201-212 (May) 1922.

[35] Morse, J. L.: Tuberculosis in Children from the Standpoint of the Pediatrist, Boston M. & S. J. **187**:463-466 (Sept. 28) 1922.

REPORT OF A CASE OF ECTOPIA CORDIS *

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Cases of ectopia cordis are sufficiently infrequent to warrant recording the following one.

REPORT OF CASE

Mrs. P. S., an Irish American, aged 43, a primagravida, first came under observation Oct. 5, 1923. The patient's family and personal history were entirely negative. She had been married less than a year at this time. Her husband had had a healthy child by a previous marriage and appeared to be in excellent health himself. The patient began to menstruate at the age of 15, which lasted for from four to five days' at twenty-eight day intervals, and was moderately profuse all her life, more so during the two years prior to the time she first came under observation; she never had any pain with menstruation. The last menstruation had occurred on April 3, quickening was noticed August 25, and the date of the expected birth was about Jan. 10, 1924.

The patient presented a blood pressure of 140 systolic, 90 diastolic, the urine was entirely negative, with a specific gravity of 1.014. Up to November 16, the blood pressure on four different occasions varied from 140 to 154 systolic, 88 to 90 diastolic. On October 27, the urine first showed a trace of albumin, specific gravity 1.023; there was no other evidence of renal involvement. Several other specimens gave the same analytic results. She was admitted to the hospital for observation on November 17, when she presented marked swelling of the feet and ankles, with some headache and visual disturbances.

Physical Examination.—The scalp and head were normal; the skin normal; the eyes reacted to light and in accommodation; the conjunctivae were pale; the extra ocular movements were normal; the ears and nose were normal; the mouth showed a degree of gingivitis; the teeth were fairly well cared for; the pharynx was slightly congested; the tongue was clean; the muscular movements were normal. The neck showed no adenopathy. There were visible pulsations of the great vessels in the neck. There was no palpable enlargement of the thyroid. The lungs were normal except for a few scattered râles at the bases posteriorly. The point of maximum impulse of the heart was in the fifth interspace, 3½ inches (8 cm.) from the midline; the sounds at the apex were regular, of fair muscular quality with no murmurs; at the right base a blowing diastolic murmur was heard, transmitted to the left and distinctly heard in the fourth interspace at the border of the sternum. The abdomen was uniformly distended and tense; the fetal parts were palpable, but no fetal heart sounds could be made out. The extremities were markedly edematous below the knees.

Roentgenogram showed a shadow of the fetal skeleton with the skull in the upper left quadrant.

On November 21, the urine showed a specific gravity of 1.020, a trace of albumin, a large number of pus cells, epithelial cells and a few granular and hyaline casts. On November 22, the specific gravity was 1.018, with increasing albumin, a few pus cells and a few granular and hyaline casts.

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* Received for publication, April 2, 1924.

* From the Laboratory and Obstetrical Division of the Jersey City Hospital, Jersey City, N. J.

Blood pressure range: November 19, 130 systolic, 70 diastolic; November 22, 140 systolic, 90 diastolic; November 24, 142 systolic, 86 diastolic; November 26, 150 systolic, 88 diastolic.

The pulse was from 100 to 120; the temperature was normal; the respirations from 24 to 34.

Renal function test, November 18, showed 10 per cent. the first hour and 15 per cent. the second hour.

The blood chemistry on November 19 showed nonprotein nitrogen 32 mg. per hundred cubic centimeters of blood, urea 12 mg., creatinin 1.7 mg., sugar 76 mg.

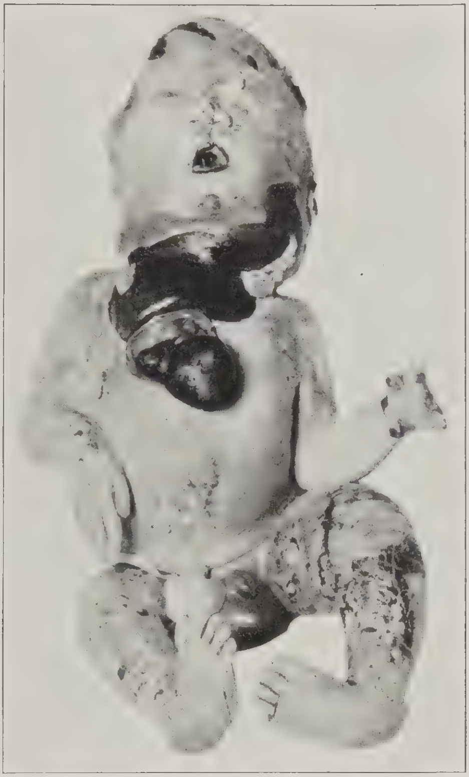

Fig. 1.—The body of the distorted fetus.

On November 26, at 5 p. m., labor was induced by the insertion of a Number 4 Voorhees bag, as the indication was the presumptive death of the fetus in utero and increasing toxemia of the patient, in spite of hospitalization and treatment. At 10:30 a. m. the following day, delivery of a stillborn fetus was effected by median forceps application.

The patient's convalescence was uneventful, the blood pressure gradually falling and the subjective evidences of toxemia entirely disappearing. The patient was discharged from the hospital on December 13.

Necropsy (November 27, 3 p. m.).—The body was that of a very much distorted and somewhat macerated fetus, measuring 37.5 cm. in length and weighing about 4½ pounds (2,041 gm.). There was an extensive swelling, reaching from the lower jaw around the neck and downward over the sternum, most marked toward the left side, and giving the appearance of the head attached directly to the thorax, without an intervening neck. The skin of the entire body was reddish, most pronounced in the region of the head and neck, and the epidermis was peeled off in part. The heart and a portion of its vessels lay free on the chest wall. The forearms were tightly flexed on the arms, appearing as marked contractures, and the ventral surfaces of the hands were whitish, softened and partially macerated. The left ear presented a similar but more advanced macerated appearance. About 2 cm. of umbilical stump was still attached. The fontanels were depressed and the cranial sutures approximated. The eyes and ears were normal. The vault of the mouth contained a complete fissure, exposing the nasal fossae. The heart was found lying in a bed formed by a depression in the chest. Both lower extremities showed an equinovarus. The diaphragm reached the fourth rib on both sides. The scrotum was markedly swollen.

The peritoneal cavity was free from fluid and adhesions. The intestines were collapsed and, on examination, contained only a small quantity of mucus; they were patent. The rectus muscles were somewhat diastatic, but there was no distinct epigastric hernia. The adrenals showed no gross lesions. The kidneys were lobulated, but otherwise grossly normal; the pelves and ureters were normal. The bladder was contracted and smooth. The pancreas, spleen and liver showed no gross lesions. Both testicles were in the inguinal canal.

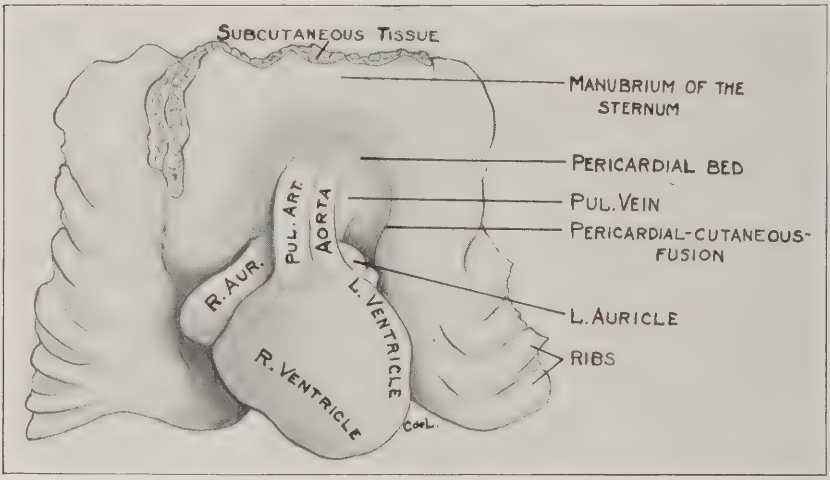

Fig. 2.—The heart as presented on the chest, showing anatomic details.

The ventral thoracic wall, lungs and heart were removed en masse. The lungs on the outer surfaces showed some atelectasis; the pleural cavities were normal. Some thymic remains were found behind the pericardial membrane. The heart was found lying in a bed formed by the depression caused by the fissured sternum, which was lined by pericardial membrane. The pericardium, as it advanced anteriorly, was apparently fused with the skin of the anterior chest wall. The sternum was fissured, producing a gaping orifice through which the heart protruded. In its manubrial portion, the sternum was represented as a single bone. Examination of the heart by incising the four chambers showed them to be distinct cavities, with patent valvular orifices. The coronary vessels could not be examined. The pulmonary artery and aorta, though joined together at their commencement for a distance of about 1.5 cm., were nevertheless on incision and exploration with a probe, found to be two distinct tubes. Patency of the ductus arteriosus and foramen ovale could not be determined without destroying the specimen.

The tongue, trachea and thyroid were removed with the thoracic organs, but showed no gross abnormalities. The head was grossly normal.

COMMENT

That ectopia cordis is a rare condition is testified by the meager literature containing isolated case reports. Its relative frequency cannot be given with any approach to accuracy. Thus, during twenty years in the necropsy rooms of Bellevue Hospital, not a single case was encountered. Neither have we been able to find statistical literature in other hospital reports. In Allbutt's [1] *System of Medicine* mention is made of the rarity of the three forms of the lesion noted by Rauchfuss, namely, ectopia cordis abdominalis, cervicalis and pectoralis. Of the three, the last is said to be the most frequently encountered, and the cervical form is said to be incompatible with life. In cases where the heart is enclosed in a pericardial sac, life may continue for days; those without a sac do not live. Recently, Holmes [2] reported a case in an infant from Howland's Clinic which lived for fifteen months. At birth, a "raw" and bright red pulsating mass was found in the epigastrium. After four weeks, with constant dressing, the mass became covered by skin. Cases have been observed in this country by Holt, Jacobi and Welch. There is an excellent article with a case report by Ellis.[3] Abbott [4] gives a brief but very concise discussion of the entire subject in Osler and McCrae's System of Medicine. Ballantyne [5] cited nine cases occurring in the literature.

The lesion is produced by failure of complete development of the sternum. Embryologically, the sternum is formed from bilateral anlages, and failure of the two pieces to fuse causes a fissure sterni with malpositions, principally of the thoracic organs, especially the heart. Schwalbe [6] states that anomalies in the development of the sternum, particularly in the lower animals, is by no means rare and, thus, anomalous positions of the heart, even within the thorax, are frequently produced. It is naturally encountered most often in premature or stillborn infants.

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1. Allbutt: System of Medicine, Vol. 6, New York, The Macmillan Company.
2. Holmes, J. B.: Johns Hopkins Hospital Reports **18,** 1917.
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THE SKIN LESIONS IN MENINGOCOCCUS SEPTICEMIA *

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The skin lesions in acute infectious diseases are among the important and most easily determined clinical findings. Their cause, in some instances, has been explained on the basis of the presence of toxic substances, and in other instances it has been shown positively to be due to the presence of microorganisms. The hemorrhagic, purpuric and petechial lesions belong especially to this latter group. The demonstration of typhoid bacilli in the "rose spots," of streptococci in the skin lesions associated with streptococcus septicemia and subacute bacterial endocarditis, of tubercle bacilli in the petechiae or tuberculids seen in acute miliary tuberculosis, are the most striking examples of this type of etiology.

The meningococcemia preceding or associated with acute epidemic cerebrospinal meningitis is manifest in some cases by the appearance of skin lesions of a petechial or purpuric nature. This characteristic has gained the terms "spotted fever," "black fever" and "petechial fever" for the disease. The existence of a meningococcemia in a considerable percentage of meningococcus infections has been demonstrated many times and in the hands of many observers, both by cultures and smears. Andrewes,[1] in 1906, Coles,[2] in 1915, King,[3] in 1918, and many others have shown the organisms in blood smears.

The study of the skin lesions is less frequently reported. Benda,[4] in 1916, studied three cases of meningitis with petechiae, in which he found a purpuric condition, and inflammatory foci with polymorphonuclear infiltration about the arterioles. In one of these cases, the most fulminating in character, he found groups of gram-negative cocci which he thought were meningcocci.

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* Received for publication, April 2, 1924.

* From Department of Pathology, Harvard Medical School, and The Children's Hospital.

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2. Coles, A. C.: Cerebrospinal Meningitis; Meningococci Found in Peripheral Blood Films, Lancet **1**:750 (Jan.) 1915.

3. King, W. W.: Early Diagnosis of Cerebrospinal Meningitis by the Examination of Stained Blood Films, J. A. M. A. **71**:2048 (Dec. 21) 1918.

4. Benda, C.: Mikroskopische Befunde in der Haut bei Petechialer Meningokokken-meningitis, Berl. klin. Wchnschr. **53**:449 (April 24) 1916.

Pick,[5] in 1916, demonstrated typical meningococci, either free or intracellular, in the skin arterioles, in the capillaries and perivascular leukocytic infiltration. He also observed the extravasation of red blood cells.

Renault and Cain,[6] in 1920, described the skin lesions in detail. They mentioned marked pericapillaritis, swelling of the endothelial cells, many of which were free in the lumina, together with many polymorphonuclears. In spite of the alteration of the intima there was no tendency to thrombosis. Congestion but not hemorrhage was present. Numerous diplococci were demonstrated in the lesions.

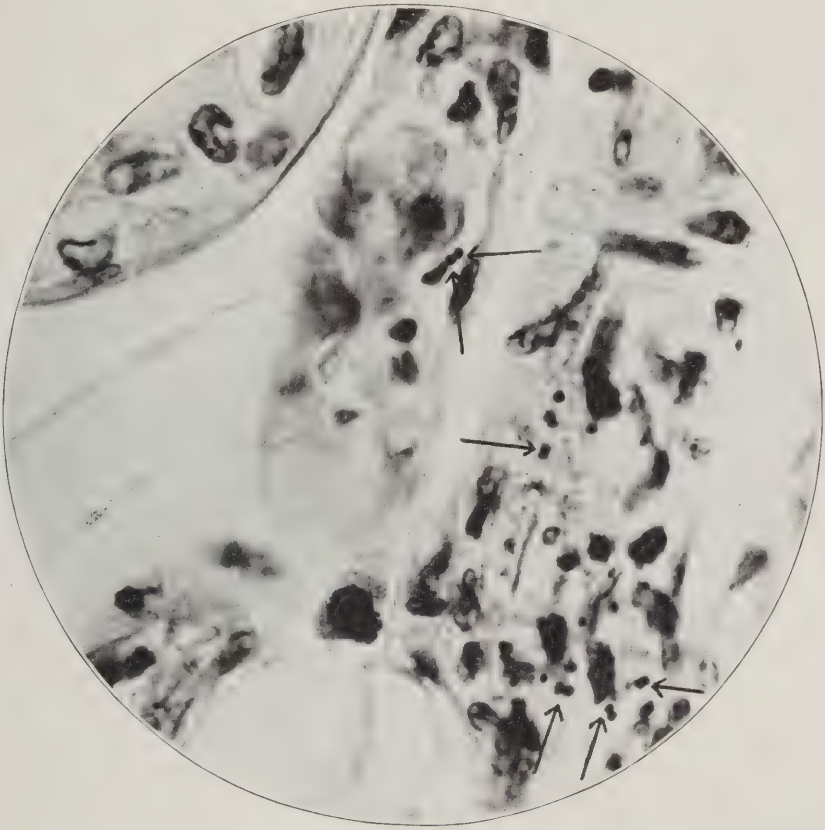

Fig. 1.—Capillaries surrounding coil gland. Several pairs of extracellular meningococci are seen. The arrows point toward the meningococci.

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[5] Pick, L.: Histiologische und Histiologisch-bacteriologische Befunde beim Petechialen Exanthem der Epidemischen Genickstarre, Deutsch. med. Wchnschr. **42**:994 (Aug. 17) 1916.

[6] Renault, J., and Cain, A.: Preuves histologiques et bacteriologiques de l'origine septicémique de purpura de la méningite cérébrospinale, Ann. de méd. **7**:114, 1920.

REPORT OF CASE

The case from which the studies reported here were made, is that of a girl, aged 2 years, who was taken acutely ill, with headache and vomiting of less than two days duration at the time of admission. Physical examination was essentially negative except for a stiff neck, hyperemic nasopharynx, a temperature of 104 F., and a skin condition not unlike a measles eruption over the face and extremities. The trunk was comparatively free of lesions. The eruption rapidly changed to large purpuric spots, and the child died a few hours after admission. Blood cultures made during life yielded pure cultures of meningococcus, as proved by morphologic and cultural characteristics supplemented by a positive agglutination reaction with antimeningococcic serum. The spinal fluid was clear and the cell count was not increased.

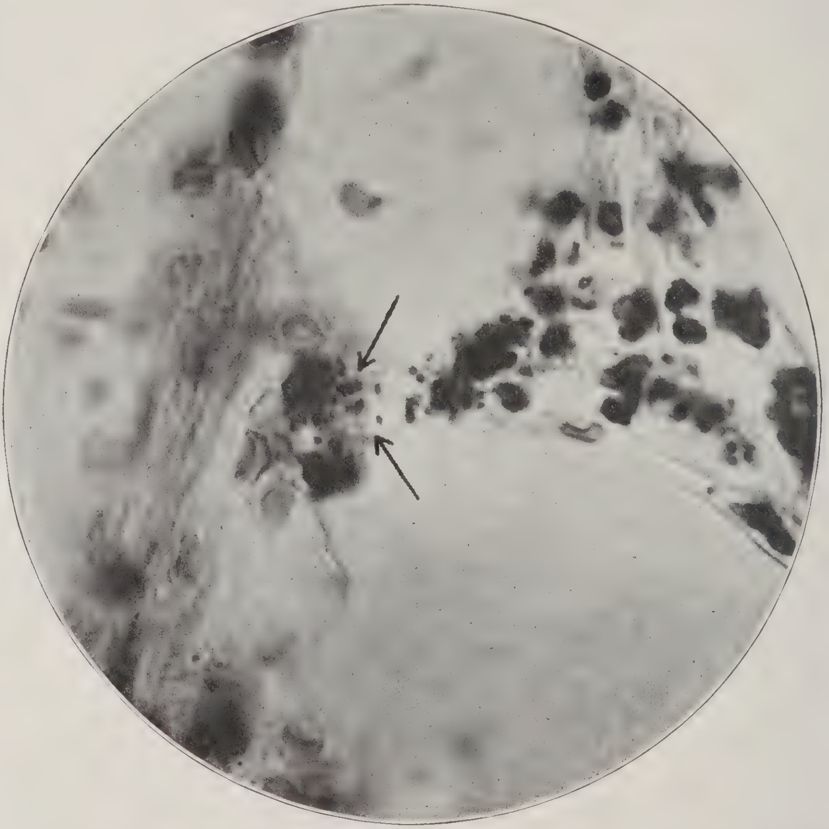

Fig. 2.—Capillaries in subcutaneous stratum. Numerous meningococci are seen in the adjacent fat. Arrow points toward the meningococci.

Restricted necropsy did not permit examination of the central nervous system, but there was no evidence of meningeal involvement by lumbar puncture. The skin lesions were the most remarkable of those found. The epidermis was entirely negative. The arterioles and capillaries in the corium and subcutaneous stratum contained many polymorphonuclears and large mononuclear leukocytes; the endothelial cells were swollen and many were detached into the lumina. No definite thrombus formation was seen. There was marked inflammatory reaction in the capillaries and small arterioles and perivascular leukocytic infiltration, the infiltrating element being made up largely of polymorphonuclear and large mononuclear leukocytes. The vessels of the subcutaneous stratum (Fig. 2 and 3) and of the capillary bed surrounding the coil glands (Fig. 1) showed the most marked lesions. Especially in the subcutaneous stratum, the vessels were engorged with leukocytes, the vessel walls were densely infiltrated with leukocytes and there was hemorrhage into the adjacent fat tissue. Many intracellular and extracellular gram-negative diplococci were demonstrated in these areas, as well as in the capillaries about the coil glands, both inside and outside the vessel walls. In a few instances an endothelial leukocyte was observed to have phagocytized one or more pairs of diplococci.

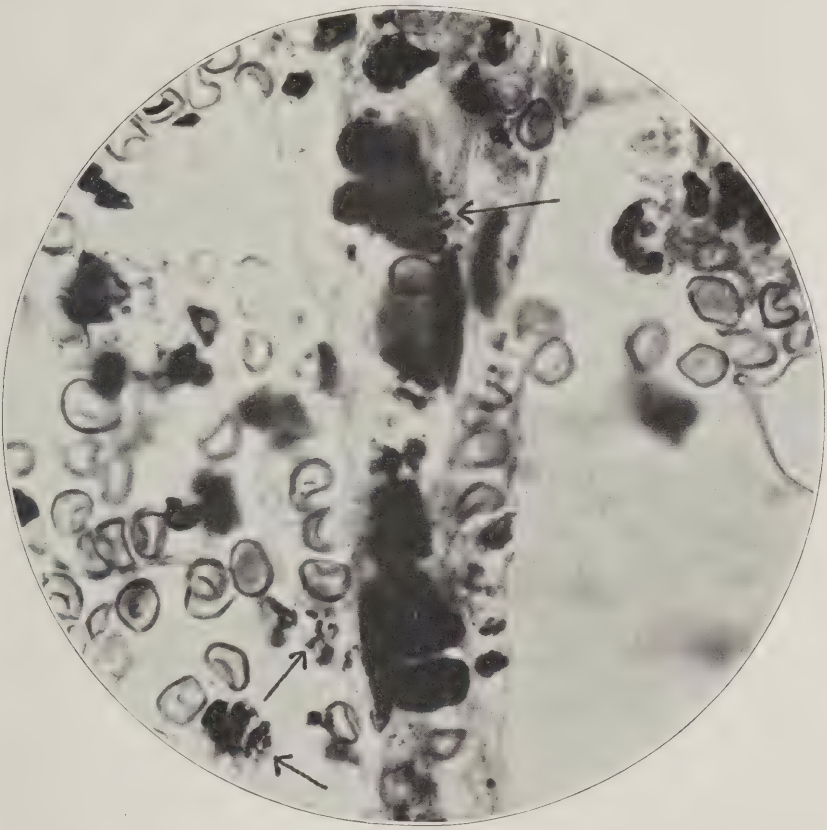

Fig. 3.—Capillaries in subcutaneous stratum, showing engorgement with leukocytes, capillaritis, hemorrhage and numerous intracellular and extracellular meningococci. The arrows point toward the meningococci.

In the other organs the mucosa of the larynx presented the greatest number of organisms. A few were found in the lungs and spleen, but none were found in the liver, kidneys, pancreas, adrenals, gastro-intestinal tract or mesenteric lymph nodes.

The histologic methods used consisted of fixation of the tissue in Zenker's fluid, paraffin imbedding, and staining of the sections by Wolbach's modification of Giemsa's method. We have found this method very satisfactory for demonstrating bacteria in tissues. These sections were controlled by staining similar sections by Gram's method, and no gram-positive organisms were found.

COMMENT

An attempt to explain the apparent localization of microorganisms in the skin in cases of septicemia would be purely a speculative one, but would have to do probably with such factors as an extensive capillary bed, slower circulation, and the provision by the skin of a temperature more optimal for the growth of microorganisms. The fact that they are more easily demonstrated in the skin makes possible a method of early diagnosis, as has been emphasized by Netter and Salanier,[7] when they demonstrated meningococci in smears of the blood and tissue juices made from the purpuric areas. The cases presenting the skin lesions are often of a rapidly malignant character, and an earlier diagnosis, therefore, of a disease which responds to serotherapy may provide a way to more intelligent treatment and possible cure, whereas delayed diagnosis may result in the death of the patient.

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7. Netter, A., and Salanier, M.: Présence des méningocoques dans les éléments purpuriques de l'infection méningococcique, Compt. rend. Soc. de biol. **79**:755 (July 22) 1916.

CEREBROSPINAL MENINGITIS WITH PURULENT IRIDOCHOROIDITIS WITH RECOVERY *

REPORT OF A CASE

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The following case of cerebrospinal meningitis is presented as evidence of the striking effect of specific serum therapy not only on the disease itself, but also on one of the less common complications.

REPORT OF CASE

E. A., a girl, aged 18 months, whose father and mother are both healthy and born in the United States, was referred from the New York City Department of Health, Oct. 29, 1923, for admission to the Babies' Hospital and was under observation on the service of the late Dr. L. Emmett Holt for thirty-three days.

The patient was the youngest of four children; the others were apparently normal in every respect. Prior to the onset of the present illness the patient had been healthy, well nourished and well developed. She had been nursed for nine months, with supplementary feedings of cereals and fruit juice at six months. At nine months she was given a liberal balanced dietary.

Previous History.—Eight days prior to admission the child became acutely ill with fever, diarrhea and repeated vomiting. She became drowsy and, according to the mother's statement, slept almost continuously for three days. Four days after the onset the drowsiness entirely subsided and irritability and restlessness, both diurnal and nocturnal, persisted for the three ensuing days. On the sixth day the elevation of temperature, which had continued from the onset, rose to 105 F. and "black spots" made their appearance on the face and buttocks. Coincident with the appearance of the eruption it was noted that the child cried out whenever an attempt was made to change her position in bed and that she seemed to have great pain, especially in the neck, when her upper extremities were moved. On several occasions, on the sixth and seventh day after the onset, the mother noted that the eyes turned backward in the child's head and it was believed that she was having convulsions. Several of these "spells" occurred during the forty-eight hours prior to her admission to the Babies' Hospital, eight days after the onset of symptoms.

Physical Examination.—On examination the child was found to be moderately well nourished and well developed. She was semicomatose and could be aroused only with difficulty. A well marked purpuric eruption was present. This was most marked on the face, about the hips and shoulder girdle with a few spots irregularly distributed over the rest of the body. There was one spot the size of a dime on the hard palate. One large ecchymotic area 2 inches (5 cm.) in length, which subsequently became gangrenous, was present on the right side of the nose; there was also a smaller area on the buttocks, which also became gangrenous. Most of the petechial spots were the size of millet seeds, but there were many larger and a few of smaller size. The character of the eruption is well shown in the illustration.

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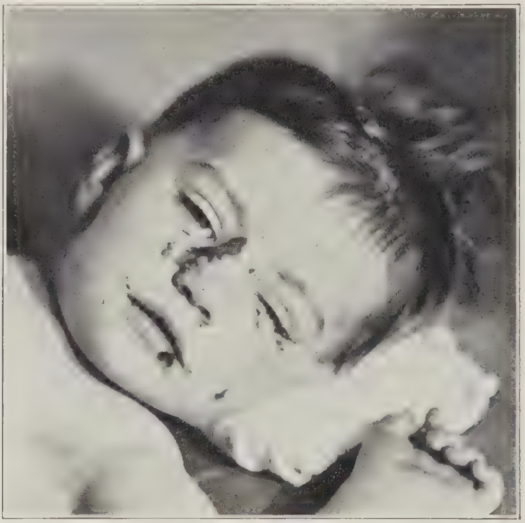
* Received for publication, April 9, 1924.

* From the Babies' Hospital.

The cornea of the left eye was markedly congested and the iris somewhat cloudy. There was no discharge. The right eye was normal. The tonsils were markedly enlarged and deeply injected. The heart and lungs were apparently normal. The abdomen was soft, and both spleen and liver could be palpated about 2 cm. below the costal margin. The anterior fontanel was about the size of a quarter and markedly bulging. The neck was rigid, the knee jerks were exaggerated and the Kernig and Brudzinski signs were both positive. The superficial lymph nodes were not enlarged.

Laboratory Examination.—Lumbar puncture was performed directly after the child's admission to the hospital, and 15 c.c. of cloudy cerebrospinal fluid was withdrawn under considerable pressure. The fluid contained 4,460 cells per cubic centimeter; the reaction for globulin was positive and the test for sugar negative. The smear revealed a great number of gram-negative diplococci, more of which were extracellular than intracellular. Blood examination showed 3,288,000 erythrocytes, 29,600 leukocytes of which 70 per cent. were polymorphonuclear neutrophils, 23 per cent. lymphocytes, 3 per cent. mononuclear leukocytes and the balance transitionals. The urine had a faint trace of albumin and a marked reaction for acetone; it was otherwise normal. Subsequent examinations of urine during the child's period of hospitalization were entirely normal.



Petechial eruption of face, with gangrenous lesion on right side of nose. (Taken on day of admission to Hospital.)

It was decided to treat the disease with liberal amounts of antimeningococcus serum intravenously, combined with active spinal drainage and intraspinal serum administration. The table shows the amount and route of introduction. Both New York State and New York City Department of Health antimeningococcus serum was used.

Two days after admission, Dr. Martha Wollstein, the hospital pathologist, reported that the culture from the spinal fluid removed the preceding day showed a growth of Type 2 meningococci. (All subsequent laboratory examinations were done under the direction of Dr. Wollstein.) Blood taken at the same time for culture showed two days later many Type 2 meningococci. A routine Wassermann test was negative.

Clinical Notes.—The day following admission the general condition of the patient revealed no apparent change, but careful examination of the skin showed that no new petechial spots had appeared. On the third day the patient was less drowsy and could easily be aroused. From then on improvement was extremely rapid; by the sixth day the child became active, recognized objects and was obviously conscious of her environment. On the ninth day she recognized her parents, showed great interest in her food and responded to questions.

Slight rigidity of the neck was still present on the tenth day, but after a few days it entirely subsided. On this date the petechial eruption, with the exception of the two larger areas, one on the face and one on the buttocks, had entirely disappeared. The slough from these two areas exfoliated at the end of the second week. On the nineteenth day the right pre-auricular gland, which drained the gangrenous area on the nose, became swollen and tender. Coincident with the appearance of the adenitis there was a rise of temperature which persisted for several days.

Amount and Route of Injections of Antimeningococcus Serum

Date	Color	Pressure	Cells	Globulin	Sugar	Serum	Intraspinal, C.c.	Intravenous, C.c.	Spinal Fluid Chemistry per 100 C.c.
Oct. 29	Cloudy	++	4,460	+	—	State	20	25	Sugar 28 Chl. 725
Oct. 30	....	....	.....	..	..	State	20	1 a.m. 25 9 a.m. 20	
Oct. 31	Cloudy	++	1,500	0	±	City	20	20	Sugar 64 Chl. 738
Nov. 1	Cloudy	++	560	+	±	City	20	20	Sugar 63 Chl. 713
Nov. 2	Turbid	+	222	+	—	City	12	..	Sugar 57 Chl. 713
Nov. 3	Clear	0	92	+	+	City	15	..	....
Nov. 6	Clear	+	72	Trace	++	.....	..	..	....
Nov. 8	Clear	+	8	—	+++	City	20	..	Sugar 71 Chl. 700
Nov. 9	Clear	+	1,540	+	++	City	20	..	Increase in cells due to meningeal reaction to serum
Nov. 15	Clear	+	9	+	+++	.....	..	..	Sugar 49 Chl. 713
Nov. 18	Clear	+	20	—	++	.....	..	..	....

Complications.—On the day of admission it was noted that the iris of the left eye was markedly congested and the cornea cloudy. The second day the condition remained unchanged. The day following the corneal cloudiness had increased and the ciliary circulation seemed more congested. It seemed apparent that pus was forming in the anterior chamber. Dr. E. S. Thomson, who made an opthalmoscopic examination on the fourth day, and all subsequent examinations, made the following report: "There is no ciliary congestion and the conjunctiva is normal. There is marked lymph exudate in the anterior chamber from the iris and also through the pupil; the tension of the eye is slightly subnormal. There is evidently a purulent infection of the choroid extending to the iris and ciliary body. It is unusual in these cases to find iris exudation, and the appearance argues for a rapid virulent process. Panopthalmitis may possibly supervene. Diagnosis: purulent iridochoroiditis." Two days later it was noted by the attending staff that the gross appearance of the left eye had greatly improved. On the tenth day after admission it was observed that the iris was free from exudate but still somewhat discolored. There was a slight fundus reflex suggesting that most of the plastic exudate was in the anterior part of the vitreous chamber. On the fourteenth day after admission, examination revealed that the vitreous was steadily clearing up. The reflex was brighter and a view of the fundus was almost possible. It was thought that prognosis was good as to vision. On the twenty-sixth hospital day the ciliary circulation was clear. The exudate back of the lens had absorbed, and there remained only a considerable amount of opacities and diffuse haziness of the vitreous. A clear view of the fundus could not be obtained but there was no appearance of a choroidal exudate. The vitreous was gradually clearing. Two weeks after the patient's discharge from the hospital it was observed that there was further improvement in the eye on the nasal side. In the ciliary region there was still some exudation. The tension of the eye was normal.

Six weeks after discharge Dr. Thomson found that improvement was progressive; that the mass of exudation in the ciliary region seemed to have almost entirely disappeared and only diffuse opacities were present in the vitreous, which were gradually lessening. A satisfactory view of the fundus was not obtainable.

The day following admission, both ear drums were incised and pus obtained from both. Gram-negative diplococci were demonstrated in smear and culture. Ten days after admission a characteristic serum rash appeared. The child's general condition rapidly improved, she sat up in bed about the sixteenth day and except for general muscular weakness seemed entirely well. One month after admission she was discharged as cured. The scar due to the gangrenous area on the right side of the face was plainly visible two weeks after discharge. Two months later the child was examined at the hospital; she walked about alone, played with toys and seemed to be normal in every respect.

COMMENT

Herrick[1] noted that of his 270 cases of epidemic cerebrospinal meningitis, only 11 had panophthalmitis; the infection reaching the eye through the ciliary vessels and not the optic nerve sheaths. He further observed that the cornea becomes cloudy and the iris congested. Shortly afterward the media becomes opaque and within a few hours sight is lost. In most cases enucleation had been performed, with resulting great improvement in the general condition of the patient. On microscopic examination the enucleated eyes showed meningococci in astonishingly large numbers. In a great number of cases mild congestive optic neuritis and retinitis were present in some degree and were a valuable sign toward early diagnosis.

In no case on record available to us has there been any report of complete restoration of vision after such an extensive invasion of the eye by the meningococcus. When the process has advanced to the stage of clouding of the transparent media, total destruction of the globe usually results. In a few cases the process has been arrested, but complete absorption of all products of inflammation has, we believe, never before been placed on record. The favorable result in the case herein reported is attributed by us to the vigorous treatment with antimeningococcic serum given by the intravenous as well as by the intraspinous route.

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[1] Herrick, W. W.: Early Diagnosis and Intravenous Serum Treatment of Epidemic Cerebrospinal Meningitis, J. A. M. A. **71**:612-616 (Aug. 24) 1918.

Cases of this character illustrate the important factor of invasion of the blood stream in meningococcic infection; a point brought out so clearly by Herrick and his co-workers in the study of the initial stages of the disease made during the epidemic in the army camps in 1917 and 1918. They further illustrate the value of the intravenous administration of antimeningococcic serum in addition to the intraspinous method. These two points in our opinion, require vigorous emphasis. It is the practice at the Babies' Hospital to administer serum both intravenously, as well as intraspinously, in all cases of meningoccic infection.

PYLORIC HYPERTROPHY IN HYPERTROPHIC PYLORIC STENOSIS *

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Investigators have disagreed widely as to the relative size of the muscularis of the pylorus in the fetus, in the full term infant, and in the infant with pyloric stenosis. In their studies of the fetal pylorus Erich Moeller,[1] Jonnesco,[2] and A. Retzius [3] found the muscularis exceptionally prominent. In the fetus there is no pyloric valve as there is in the adult, and closure occurs by a contraction of the entire pyloric segment, which is known in the anatomic literature as the canalis pylori. They found the proximal boundary of the pyloric canal more or less indistinct, whereas the distal demarcation is usually rather sharp. In three premature infants Ibrahim [4] reported the muscularis of the pyloric canal thicker than that of the full term normal infant. Wachenheim [5] came to the conclusion that the diameter of the fetal pyloric musculature is often greater than that of infants a few weeks old. This he believes to furnish an "anlage" for subsequent hypertrophy. According to this author, a persistence of this transient, normal condition gives a primary, anatomic basis for the origin of stenosis. If a disproportion in the antagonistic circular and longitudinal muscle layer exists, the one will develop more rapidly than the other and hypertrophy with its secondary symptoms of obstruction results. Hertz [6] failed to find the muscularis of the pyloric canal thicker in the fetus and prematurely born infant than in the full term infant. He considers a diameter of 448 to 672 microns, values which Fröhlich [7] found for prematurely born infants,

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* Received for publication, March 1, 1924.

* From the Department of Pathology, University of Chicago, and the Sprague Memorial Institute Laboratory of the Children's Memorial Hospital, Chicago.

1. Mueller, E.: Beiträge zur Anatomie des menschlichen Foetus, K. Svenska Vetenskaps, Ak. Handl. **29**: Vol. 2, 1897.

2. Jonnesco: Traité d'anatomie humaine, Poierier **45,** 1895.

3. Retzius, A.: Bemerkunken über das Antrum pylori beim Menschen, Müller's Arch. **1**:74, 1857.

4. Ibrahim, J.: Die angeborene Pylorusstenose im Säuglingsalter, Berlin, 1905; Die Pylorusstenose der Säuglinge, Ergebn. d. inn. Med. u. Kinderh. **1**:208, 1908.

5. Wachenheim, F. L.: Pyloric Hypertrophy in New-Born Infants, Am. J. Dis. Child. **10**:87 (Aug.) 1915.

6. Hertz, P.: Ueber die angeborne Pylorusstenose des Säuglings., Jahrb. f. Kinderh. **72**:32, 131, 1916.

7. Fröhlich, T.: Om Pylorusstenose hos spaedbarn, Norsk. Mag. f. Laegevidensk. **4**:1046, 1906.

equal to that for full term infants. Cunningham,[8] on the contrary, claimed that this part is less developed during the last months of fetal life than in the new-born.

That the state of contraction of the normal stomach influences the thickness of its various parts is emphasized by Pfaundler.[9] He distinguishes a contracted or "systolic," from a relaxed or "diastolic" stomach and he maintains that a water pressure of 30 cm. will change the systolic into the diastolic type. He was probably the first to demonstrate the similarity in anatomy of the normal, systolic stomach and the hypertrophic pyloric stenosis stomach. Both have a thick muscle layer, deep rosette like folds of mucosa, and absence of a pyloric valve. The distal end of both is irregular, i. e., it is often longer at the greater than at the smaller curvature. This irregularity is caused by the diagonal course of the sulcus pyloricus. In both, the muscularis of the pyloric canal increases distally, reaching its greatest thickness at the end of the greater curvature. The chief difference between the normal systolic pylorus and the stenosed pylorus is an increase in muscularis of the latter. Pfaundler found the greatest thickness of the normal systolic pylorus to be 3 mm., that of the hypertrophic stenosis cases to range from 3.5 to 5 mm. Very recently, Wernstedt [10] has again asserted that to study the true thickness of the muscularis one must establish the "ground form" before the specimen is fixed and sectioned. He accomplishes this by exerting a water pressure of 30 cm., or more, on the immersed stomach. If the mucosal folds are thus obliterated there is no hypertrophy. Employing this preliminary technic he found the normal pyloric muscularis to average only 1 mm. in thickness; that of the hypertrophic pyloric stenosis cases to vary from 1.5 to 2.5 mm.

Most investigators report the hypertrophy to involve the circular muscle layer; Finkelstein,[11] however, reported a case in which the longitudinal layer was hypertrophied, and he and Gran state that all the layers of the pyloric wall may be hypertrophied. Bernheim,[12] Peden,[13] Wernstedt,[10] and Ibrahim,[4] who have made microscopic studies of the muscle bundles, cells and nuclei, all agree that the individual muscle cells and nuclei are larger in the hypertrophic pylorus cases than in normal, contracted stomachs. They interpret their findings as proof of a true hypertrophy of the individual muscle cells.

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[8] Cunningham, J.: The Varying Form of the Stomach in Man and the Anthropoid Ape, Tr. Roy. Soc. Edin. **45**:1, 1906.

[9] Pfaundler, M.: (Pylorusstenose im Säuglingsalter), Pfaundler-Schlossmann, Handbuch der Kinderkrankheiten **2**:181, 1906; Beiträge zur Frage der Pylorusstenose im Säuglingsalter, Jahrb. f. Kinderh. **70**:253, 1909.

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[11] Finkelstein, H.: Ueber angeborene Pylorusstenose im Säuglingsalter, Jahrb. f. Kinderh. **43**:105, 1896; Berl. klin. Wchnschr. **43**, 1897.

[12] Bernheim: Ueber Pylorusstenose im Säuglingsalter, Cor.-Bl. f. schweiz. Aertze **8**:257, 1904.

[13] Peden, W.: Case of Congenital Stenosis of the Pylorus in an Infant, Tr. Glasgow Path. & Clin. Soc. **3**:193, 1892.

The extensive, accurate measurements of the muscularis of the pylorus by Hertz [6] deserve consideration. He found, for example, that the diameter of the muscularis in two normal infants was 2,380 and 2,550 microns respectively; in some of his seventy newborn and prematurely born infants it reached 2,550 and 2,770 microns; and in his six pyloric stenosis cases it varied from 2,720 to 5,100 microns. These measurements show that in some of the normal and prematurely born infants the diameter of the pyloric muscularis approximated the lowest values found in the hypertrophic stenosis cases.

In spite of the fact that macroscopic inspection of the pylorus, accurate measurements of the diameter of the muscularis, and cytologic study of the muscle cells and their nuclei tend to show the existence of hypertrophy in stenosis cases, a number of investigators [14] question the existence of an actual increase in the muscle layer. Thus Pfaundler [9] takes the stand that the pylorus in these cases is merely in a state of spasm, and Haas [15] believes "hypertrophic pyloric stenosis to be an advanced degree of pylorospasm." Mohr [16] questions the validity of microscopic measurements in determining pyloric hypertrophy. The marked variations given by Hertz [4] and others for the thickness of the pyloric muscularis not only of stenosis cases but also of the normal, systolic pylorus make him ask: "When is a pylorus hypertrophied?" He reiterates that a micron is a very small unit of measure, that it is difficult to section specimens in exactly the same plane, and that it is almost impossible to obtain two stomachs in the same stage of contraction. Pfaundler [9] raises the objection that most of the microscopic studies have been based on material hardened in formaldehyd, and Aschoff [17] has demonstrated the marked influence of fixing fluids on the contraction of the pylorus.

The existence of the objections noted in the preceding paragraph, and the more or less conflicting data as furnished by accurate measurements, suggested to the author another line of attack in an attempt to prove definitely the existence of hypertrophy in pyloric stenosis. For this purpose wax models were prepared of the muscularis of two pylori of infants of the same sex, approximately the same birth weight, and practically the same age at the time of death. The control pylorus was that of an infant who died of peritonitis resulting from a ruptured appendix, the other one that of an infant who died of bronchopneumonia complicating a hypertrophic pyloric stenosis.

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[14] Sauer, L. W.: Hypertrophic Pyloric Stenosis—A Monographic Review, Arch. Pediat. **41**:145 (March) 1924.

[15] Haas, S. V.: Congenital Hypertrophic Pyloric Stenosis and Its Treatment by Atropin, J. A. M. A. **79**:1314 (Oct. 14) 1922.

[16] Mohr, M.: Ein Beitrag zur Frage des reinen Pylorospasmus, Ztschr. f. Kinderh. **29**:111 (June) 1921.

[17] Aschoff, L.: Engpass des Magens, Jena, 1918.

REPORT OF CASES

CASE 1 (Control).—F. P., a boy, was born at full term, September, 1922. The birth was normal, the weight was 3,050 gm. The child was nursed until the fatal illness which began five days before death. The weight was 2,820 gm. at the time of death, which occurred on the fifty-fifth day. Pathologic diagnosis: Appendicitis and peritonitis.

CASE 2.—(Hypertrophic pyloric stenosis).—J. W., a twin boy, was born September, 1922. The birth was normal, the weight was 2,800 gm. The child was nursed until a few days before death. The weight was 2,500 gm. at the time of death, which occurred on the fifty-second day. Clinical and pathologic diagnosis: Hypertrophic pyloric stenosis and bronchopneumonia.

The specimens taken from these cases, were selected from a collection of thirty infants' stomachs, and fixed in the following manner shortly after death. After the duodenum was tied off a few centimeters below the pylorus, the esophagus was cut a few centimeters above the cardia and the stomach contents expressed through the cardia. The stomachs were rinsed with Müller's fluid, and then were filled to capacity with the fluid; finally the esophagus was securely tied and the specimens were immersed in the fixing fluid.

After a few weeks the two specimens were removed from the fixing fluid, the pylorus was dissected from the rest of the stomach, and the two pylori were passed simultaneously through the various dilutions of alcohol, ether, and celloidin. They were then embedded in the same block of celloidin. The serial, longitudinal sections of 50 microns thickness were then stained with alum-hematoxylon and counterstained with acid fuchsin according to the Van Gieson method. There were 163 control sections and 238 sections from the stenosed pylorus. Tracings of the outline of the muscularis of each section were prepared with the aid of an Edinger projection apparatus at a magnification of twenty diameters. Finally, serial wax plates of 2 mm. thickness were prepared of every other section according to Born's method, and the muscularis of the pylorus was then reconstructed from the serial wax plates.

A glance at Figure 1 shows a distinct difference in the size of the two stomachs. The stenosis specimen is 5 cm. longer, 4 cm. wider at the cardia, and its capacity exceeds by 17 c.c. that of the control. It differs appreciably from the specimens examined by Hertz[6] and Wernsted[10] (Table of Data). Hertz found the size in most of the cases he examined to vary little from the normal, only three being distinctly enlarged; the largest he studied had the following dimensions: greater curvature 31 cm., smaller curvature 7 cm., length 12.5 cm. and width 7 cm. Wernstedt found enlargement in none of the seventeen cases that he studied. Ibrahim,[4] Feer,[18] Pfaundler [9] and Adler [19] frequently found dilatation present. Hertz,[6] Hirschsprung,[20] Ibrahim [4] and Wernstedt [10] often found the muscularis of the entire stomach thicker than normal. This increases in diameter, as pointer out by Wernstedt, may be influenced by the state of contraction.

Inspection showed the cylindric, pyloric canal present in both specimens. The incisura angularis separated the pylorus proximally from the vestibulum (antrum), and the sulcus pyloricus marked it off sharply from the duodenum. Palpation aided in the determination of the distal boundary of both pylori, and inspection of the gastric mucosa was of value in locating the exact transition from vestibulum to pyloric canal, especially in the stenosis specimen, for the difference in width was greater and the gastric mucosal folds were absent (Fig. 2). The length measurement of the pyloric canal was made along a line equidistant from the smaller and the greater curvature. This is, in a sense, the average length, as the canal was found a few millimeters shorter at the smaller curvature, because of the diagonal, downward course of the

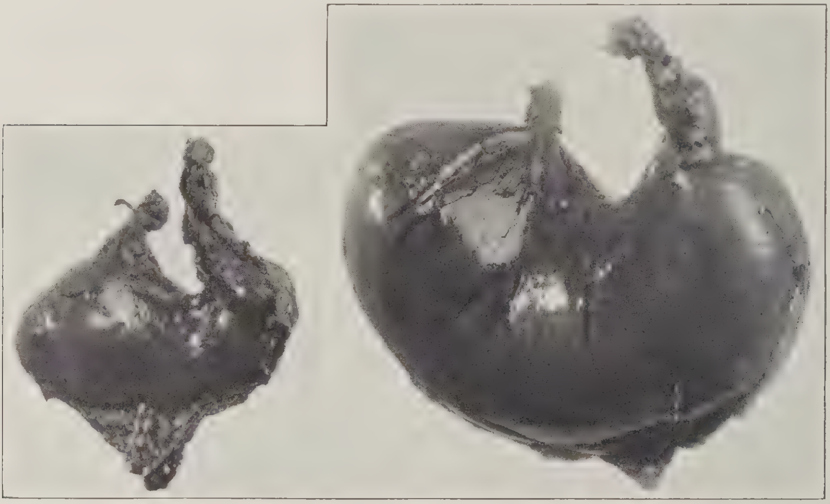

Fig. 1.—Dorsal view of the two stomachs; *a*, control case, *b*, stenosis case.

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[18] Feer, E.: Verh. Ges. Kinderheilk., Stuttgart, 1906.

[19] Adler, M.: Ein Fall von angeborener funktioneller Pylorushyperplasie, Jahrb. f. Kinderh. **17**:197, 1908.

[20] Hirschsprung, H.: Fälle angeborener Pylorusstenose. Jahrb. f. Kinderh. **28**:61, 1888.

sulcus pyloricus from the smaller to the greater curvature. The cartilage-like specimen is somewhat curved, with its convexity along the great curvature. The control specimen measured 18 mm., the stenosed pylorus 23 mm. Hertz found the pyloric canal of the newborn to measure from 12 to 18 mm., that of stenosis cases to vary from 15 to 30 mm. with an average of 20 mm.

Microscopic examination of the stained, longitudinal sections of both pylori (Fig. 3) showed the presence of four layers: (1) Tunica serosa (visceral peritoneum); (2) tunica muscularis, consisting of: (*a*) an outer, longitudinal layer (stratum longitudinale); (*b*) an inner, circular (stratum circulare); (3) tela submucosa, an appreciable layer of loose connective tissue, elastic fibers, fat, and blood vessels, and (4) tela mucosa, the thin, innermost layer of mucous membrane.

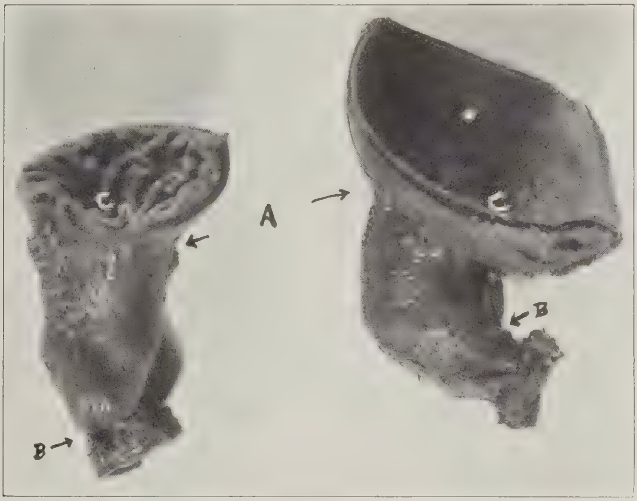

Fig. 2.—Control and stenosis pylori, showing *a*, incisura angularis; *b*, sulcus pyloricus; *c*, vestibulum (antrum) pylori.

The striking difference in the two specimens was the marked increase in the stratum circulare of the tunica muscularis in the stenosis specimen (Fig. 3). The greatest diameter of the tunica muscularis measured 3,850 microns; that of the control specimen was 2,500 microns. Hertz found the diameter in his stenosis cases to average between 3,000 and 4,000 microns, although in one instance it measured only 2,750 microns, a value equal to that found by Wernstedt [10] for a normal,

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21. Simon, J.: Anatomischer Magenbefund eines Säuglings fünf Monate nach Heilung von Pylorusstenose, Jahrb. f. Kinderh. **63**:331, 1911.

4 months old infant. Ibrahim [4] and Simon [21] obtained no measurements above 2,000 microns for the contracted pylorus of the normal new-born.

The mucosa was not found increased in the stenosis case. It was characteristically raised into several more or less longitudinal folds which, so far as could be determined, extended throughout the pyloric canal in both specimens. Although the mucosa and the submucosa have been reported thickened in several cases of pyloric stenosis, all of Wernstedt's sixteen cases failed to show such a variation. The results of his investigations are supported by the fact that in Figure 3 *B* the diameter of the mucosa is certainly not greater than that in the control, Figure 3 *A*. Bendix [22] holds that the mucosa may contribute appreciably to the obstruction of the lumen by producing folds which effect a valve-like closure. The diameter of the pyloric lumen cannot be accurately measured because the mucosal folds produce more or less obliteration. In fatal cases of hypertrophic pyloric stenosis, the lumen has been found to vary from the diameter of an average sized lead pencil to that of the finest sound. Hertz attempted to measure the lumen in two of his fatal stenosis cases by sectioning the pylorus longitudinally and then

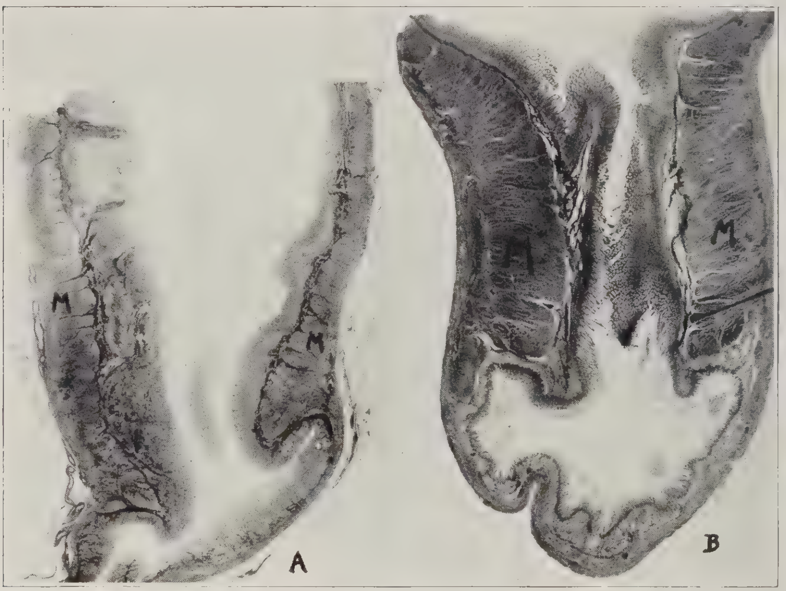

Fig. 3.—Longitudinal section of the pyloric canal; *a,* control case, *b,* stenosis case. Marked increase in muscle layer (u) in *b.*

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[22] Bendix, B.: Pylorospasmus und Pylorusstenose im Säuglingsalter, Med. Klin. **5**:1813, 1909.

stretching the specimen on a flat surface. The distance between the cut surfaces measured 18 mm. in the one instance, and 22 mm. in the other. These measurements are almost the same as those made by Pfaundler on thirteen infants, that died during the first month of life. A reduction of the lumen is, therefore, not due to a decrease in the mucosal surface.

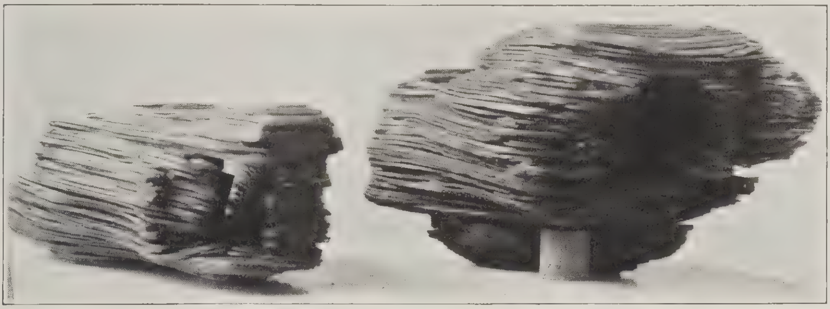

Fig. 4.—Wax models of the muscular layer of the pyloric canal; *a,* normal pylorus, *b,* stenosis case.

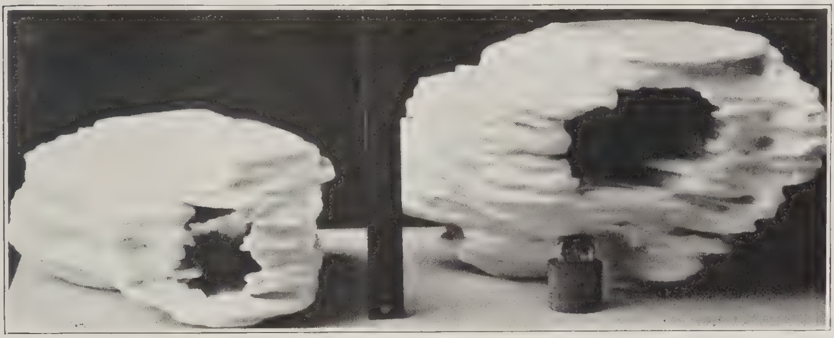

Fig. 5.—Finished models, showing contrast in size, also diameter of lumen, and thickness of the muscularis.

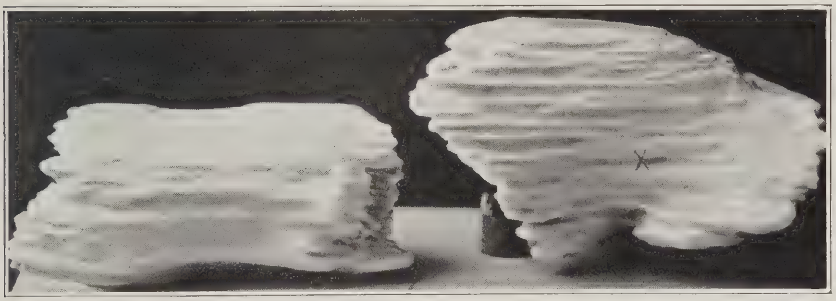

Fig. 6.—Lateral view of models, showing the shape of the hypertrophied, pyloric muscularis at X.

That an actual increase in muscularis occurs in pyloric stenosis is emphasized by a comparison of the two wax models. This evidence is more conclusive than microscopic measurements of the diameter of the muscularis, for we know that the spastic element in stenosis makes the muscularis of the pylorus contract, and its cartilage-like consistency is more likely due to the spastic contracture than to an increase in the muscle layer. Figure 4 illustrates the models of the muscularis *A* of the normal pyloric canal; *B*, of the infant with pyloric stenosis. Model *A* weighs 3,000 gm. and model *B* weighs 6,050 gm. This vast difference in bulk is conclusive evidence, as the infant with the stenosis weighed 150 gm. less at birth, never regained his birth weight, weighed approximately 300 gm. less at the time of death, and was three days younger than the control. The finished models (Fig. 5.) illustrate not only the marked contrast in size, but also the diameter of the lumen and the thickness of the muscularis of the two specimens.

A Comparative Tabulation of Data

	F. P. (Normal)	J. W. (Hypertrophic Pyloric Stenosis)
STOMACH		
State	Systole	Diastole
Capacity	37 c.c.	54 c.c.
Length	8 c.m.	13 cm.
Width at cardia	4 c.m.	8 cm.
Mucosa	Deep folds	No folds
PYLORUS		
State	Patent	Not patent
Lumen	Rosettelike folds	Deep, rosettelike folds
Consistency	firm	Cartilaginous
Length	18 m.m.	23 mm.
Circumference	38 m.m.	47 mm.
Number of sections	163	238
MODEL		
Weight	3,000 gm.	6,050 gm.
Length	30 cm.	35 cm.
Height	14 cm.	22 cm.
Median diameter	22 cm.	28 cm.
Median circumference	57 cm.	76 cm.
Thickness at antrum	2 cm.	4 cm.
Thickness at duodenum	2.5 cm.	9 cm.
Plane of lumen	Horizontal throughout	Horizontal, vertical, horizontal
Diameter of lumen at antrum	18 cm.	18 cm.
Median diameter of lumen	12 cm.	8 cm.
Diameter of lumen at duodenum	4 cm. x 7 cm.	9 cm. x 12 cm.
Form of lumen	Funnelshaped	X-shaped

A comparative study of the two models shows not only that they differ in mass, but that the form and plane of the lumina are not alike.

The so-called lumen or passageway in the control model resembles somewhat a funnel with the smaller aperture at the distal or duodenal end, whereas in the stenosis model it is narrowest near the middle, thus resembling somewhat the letter X. These differences can also be seen in the longitudinal sections (Fig. 3), but as this difference involves mainly the muscularis, it is more pronounced in the models. The measurements of the lumen at different levels (as recorded in the Comparative Tabulation of Data), verify this point. The other difference which deserves mention is the plane of the so-called lumen. In the control model it remains horizontal from one end of the pyloric canal to the other; in the stenosis model, on the other hand, it is first horizontal, then there is a rather abrupt vertical drop near the middle of the model, and from there on it continues horizontal to the distal end. Further investigation of these two striking differences may lead to a solution of the etiology of hypertrophic pyloric stenosis.

SUMMARY

1. Evidence offered as proof of hypertrophy of the tunica muscularis of the canalis pylori in infants with pyloric stenosis has been challenged by various investigators.

2. Wax models of the muscularis were prepared from serial, longitudinal sections of two pylori from male infants of approximately the same age and weight, *A* a normal pylorus and *B*, a typical stenosis of the pylorus.

3. The lumen of the control model is somewhat funnelshaped; that of the stenosis model resembles somewhat the letter X.

4. The plane of the lumen of the control model is horizontal; that of the stenosis model is horizontal, vertical, horizontal.

5. The wax model of the normal muscularis weighed 3,000 gm., that of the stenosis weighed 6,050 gm., a conclusive demonstration that a marked hypertrophy of the muscularis exists.

PROGRESS IN PEDIATRICS. REVIEW OF THE LITERATURE FOR 1923 ON INFANT FEEDING *

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BREAST FEEDING

Kuttner and Ratner [1] have undertaken to investigate the work of Theobald Smith to determine the essential nature of colostrum feeding in calves. These investigators were interested in its bearing on infant feeding. Smith showed that colostrum is not alone the chief means for transferring antibodies to the new-born calf. Colostrum also seems to have the important function of protecting the new-born animal against a general invasion by organisms of the *bacillus coli* group. With this in mind, Kuttner and Ratner sought for evidence of histologic differences in the placentas of various species. They used in their researches toxin, antitoxin and the Schick test as a means of control. There were some investigators who claimed that the placenta was impermeable to antibodies and that only through the milk was immunity transferred. In approaching this problem in human beings it was divided into two lines of study: (1) to determine the manner in which antibodies are conveyed from mother to child; comparing the antibody contents of colostrum with that of the blood of the mother, the cord blood, and the blood of the infant after the ingestion of colostrum, and (2) by clinical study of any reliable records of noncolostrum fed infants.

The result of their inquiry produced the following information. The human placenta was found, in accordance with the results of previous workers, to be penetratable to diphtheria antitoxin. Human colostrum occasionally contains small amounts of antitoxin, but this amount is always less per volume than that found in the blood serum of the mother or in the cord blood. No antitoxin was shown to exist in the colostrum. They concluded that colostrum feeding in human beings has no significance as to transferring immunity. These findings do not agree with those of Theobald Smith.

During the last year encouragement to the young mother to nurse her child has received a great deal of attention by the profession. Donnelly,[2] in an extensive article on breast feeding, discusses the

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* Received for publication, April 23, 1924.

[1] Kuttner, Ann, and Ratner, Bret: The Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

[2] Donnelly: Methods of Sustaining and Regulating the Supply of Breast Milk, Long Island M. J. **17**:13 (Jan.) 1923.

methods of sustaining and regulating the supply of breast milk. He believes that two fundamentals are necessary: (1) regular stimulus to the breasts by the suckling infant, and (2) complete emptying of the breasts at each feeding. The quantity of breast milk may be increased in four practical ways: (1) by nursing both breasts at each feeding, (2) by increasing the intake of fluids, (3) by proper exercise, short of fatigue, and (4) by securing sufficient rest at night. The solids in the milk are increased by shortening the intervals of nursing and are diminished by lengthening these intervals. He believes that the vitamin content is of great importance. He instructs the mother to take large quantities of foods that are rich in vitamins. Both Richardson[3] and Watton[4] urge that every new-born infant delivered in a hospital ward be immediately placed on the children's service, so that the pediatrist can look after the supply of mother's milk and conserve it for as long as possible. Proper campaigns should be launched to instruct mothers in the necessity of breast feeding for some months; together with the technic of breast feeding. Emphasis should be placed on the manual emptying of the breasts. The manipulation is quite similar to that employed in ordinary milking, except that approximation of the thumb and finger is substituted for the whole hand. The plea for supervision by the physician, who is interested in child welfare, is important at an early age.

Jewesbury[5] has been able to continue breast feeding in at least 95 per cent. of the cases, if not alone, at least partly. The only cases where breast feeding should not be advised is when the mother is suffering from active pulmonary tuberculosis, or any disease in which there might be rapid progressive wasting, or when she again becomes pregnant. In the presence of failing milk he puts the baby regularly to both breasts, usually at three hour intervals. In Schoedel's[6] experience the weak infant who is doing well will drink at the end of the second week from 130 to 175 gm., at the end of the third week from 140 to 190 gm., at the end of the fourth week from 145 to 210 gm., and from the sixth to eighth weeks from 150 to 250 gm., per kilogram of body weight. For a weak infant to thrive well on exclusive feeding with pumped milk it is often desirable to give him somewhat larger quantities than this. In his clinic, the children make good progress when they drink at the end of the first week from 95 to 110 gm., and at the end of the second week from 140 to 240 gm. His figures show the need for greater amounts of food for weak infants. He says that it should always be remembered that the sucking power of the weak infant is soon exhausted, and hence if put to the breast more frequently it will obtain greater amounts of food. He prefers giving the breast feeding eight times in twenty-four hours for the premature baby and decreases these to seven or six as the child develops. The advantage of more frequent stimulus to the breasts increases their function, which is endangered if the child drinks with very little force at long intervals. Weak or premature infants are usually given from eight to ten feedings.

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[3] Richardson: A Breast Feeding Campaign, Long Island M. J. **17**:9 (Jan.) 1923.

[4] Watton: Supervising Breast Feeding, Long Island M. J. **17**:14 (Jan.) 1923.

[5] Jewesbury, R. C.: Some Notes on Breast Feeding, Arch. Pediat. **40**:101 (Feb.) 1923.

[6] Schoedel, J.: The Amount and the Number of Feedings on which Weak Infants Thrive when Fed on Breast Milk, Jahrb. f. Kinderh. **102**:227 (June) 1923.

In discussing the methods for promoting the supply of breast milk Smyly [7] believes that the rules are so simple that the poorest mother can carry them out in the poorest home. This work in China has been directed to institute a simple, healthy, well regulated life amid hygienic surroundings. The mother and baby are kept in the open air and sunlight as much as possible. The mother should take morning exercises before an open window every day; this should never be carried to the point of fatigue. Alternate hot and cold sponging of the breasts should be performed morning and evening. A definite period should be arranged each day when the baby's bulky clothing can be removed, allowing the free use of its limbs. The results in two cases are reported: (1) the milk supply was reestablished after nursing had been entirely discontinued for a week, (2) a patient with low mentality and poor physique was able to nurse her child satisfactorily after following a definite program.

Birk [8] has made a study of the changes in the breast milk during lactation. He employed in his clinic the same woman as a wet nurse for three years. This gave him an opportunity to determine whether the content of nutritive material and salts still averaged the minimum physiologic requirement. He found that fluctuation in the amount of protein was insignificant. The average value of the milk fat was 5.4 per cent., lactose varied from 7.2 to 7.6 per cent. He believes that breast milk, after three years of lactation, still contains a sufficient amount of nutritive material and salts. Apparently the figures given by other authors for breast milk have habitually been made at the beginning and at the height of lactation.

The question of whether the infant may thrive better on cooked breast milk than on raw breast milk has been studied in great detail by

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7. Smyly, E.: Deficiency of Breast Milk in Nursing Mothers: Treatment, China M. J. **37**:834 (Oct.) 1923.

8. Birk, W.: Changes in Breast Milk During Lactation, Monatschr. f. Kinderh. **25**:30 (March 25) 1923.

Martin[9] and Wülfing.[10] Fifty new-born and older infants were fed on boiled breast milk. The breasts were milked alternately at the feeding time. The milk was caught in sterile vessels and put into bottles which were sterilized by boiling vigorously. As colostrum coagulates on boiling, the new-born infants were given boiled milk from other mothers until their own mothers' milk became free from flocculation. There was no noticeable thickening of the milk on boiling. The weight curves of these children were the same as those of breast fed children, or even a little more favorable. The quantity of the breast milk was increased by careful milking. This, he believes, shatters the theory that it is stimulated by sucking. Boiled breast milk is as good a food as unboiled for the normal infant. At any rate cooked breast milk does not have any unfavorable effect.

In discussing the use of complementary breast feeding Gerdine[11] feels that this method has grown popular throughout the country and is of great value. It consists of putting the infant to the breast at regular feeding times and encouraging it to nurse as completely as possible. The breasts are then emptied by the manual method, as he feels that this is vastly superior to any pump. In this way it is recognized that practically every mother can nurse her baby.

Woodbury,[12] in a study on the relationship between breast and artificial feeding as a cause of infant mortality, obtained data from eight American cities, through the Children's Bureau in Washington. The information included a record of the feedings received in each month of life for the first year. An analysis on the influence of feeding was made from data on 22,422 live born infants. The kinds of feeding were classified into three groups: (1) exclusively breast, (2) exclusively artificial, and (3) partly breast and partly artificial. The analysis showed that artificial feeding, as actually practiced in typical American city populations, is associated with a mortality of between three and four times as high as that among breast fed infants. This excess is not to be explained by the fact that the artificially fed infants form a much larger group than the others; it appears that this mortality goes through all nationalities and all earning groups, though with slight variations depending possibly on the particular conditions prevailing in each group.

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[9] Martin, E.: Boiled Breast Milk, Klin.-therap. Wchnschr. **2**:228 (Feb. 12) 1923.

[10] Wülfing, E.: Feeding with Cooked Breast Milk, Ztschr. f. Kinderh. **35**: 56 (Feb. 14) 1923.

[11] Gerdine, L.: Complemental Breast Feeding, J. M. A. Georgia **12**:4 (Jan.) 1923.

[12] Woodbury, R. M.: The Relation between Breast and Artificial Feeding and Infant Mortality, Am. J. Hygiene **2**:668 (Nov.) 1922.

ARTIFICIAL FEEDING

During the last year very little has been added to our knowledge of artificial feeding. Articles by Giffen,[13] Cowie,[14] Hoobler,[15] Mucklow,[16] Mixsell,[17] and Schmalfuss [18] have been published on this subject. They all agree that the normal infant requires 45 calories per pound of body weight, to maintain and gain weight. Whole milk mixtures with simple dilutions of plain or barley water, with the addition of sugars, seem to be most popular. Probably the greatest addition to infant feeding during the last year has been the more extensive use of lactic acid milk and corn syrup. Almost every type and combination of feeding has been tried.

In a very complete and exhaustive survey of the whole subject on the pathology and therapy of nutritional disorders in artificially fed infants Finkelstein [19] divides the cases of diarrheas into the following groups: (1) Fermentation diarrheas. These are brought about by the irritative effects of volatile fatty acids, which have a stimulating effect on the peristalsis. As compared with fermentation, putrefaction is of minor significance as an agent producing diarrheas in infants. It has been shown by clinical observations, as well as by experiments, that in fermentation we deal with a carbohydrate fermentation. The crystalline sugars, lactose above all, are particularly related to diarrheas. There is a remarkable difference between the crystalline and the colloidal carbohydrates, including flour. As regards fermentability in the intestine, polysaccharids are much more resistant to bacteria, but show a depressing influence on the velocity and intensity of sugar fermentation. He believes that fat turns the balance, increasing diarrhea when there is a tendency to fermentation, whereas it favors the formation of solid stools in the opposite case. We should never forget that in the intestinal chemistry the influence of metabolic dynamics on nutrition has a decisive significance. The same food may, under varying condition, in different children or with the same child at different times, produce a different effect. Protein is not only valued as a stimulant to fermentation, but as a buffer substance by promoting the secretion of intestinal juices. Protein, therefore, helps to neutralize acids, to accelerate the digestion and absorption. Crystalline sugars are not merely a substratum for fermentation, but show practically the identical action as in the test tube. Lactose seems to deserve the foremost rank as a substratum for enzymatic action. All things being equal, lactose has the most powerful purgative effect. It acts more intensely than the crystalline saccharose. He calls attention to the fact that the decisive factor in the origin of diarrheas is not to be found in abnormal fermentative processes. The production of abnormal acid reactions, in parts of the intestine very sensitive to acids, causes diarrheas. Therefore, an abnormal decomposition in the jejunum makes the diarrhea more intense the higher in the intestine the process of decomposition takes place; (2) Inanition diarrheas. These may occur if the food ingested is deficient in the one indispensable constituent. In infants, it is usually part of a terminal condition. In extreme atrophic children, very often during the last days of life without any particular reason, watery stools occur with an abrupt loss of weight, leading very soon to a fatal collapse. According to Finkelstein's experience this condition is relatively frequent in the first days of life, probably because of the fear of doing harm to the new-born infant by giving cow's milk in sufficient amount. The most frequent cause is possibly an insufficient ingestion of carbohydrates. At times, even a slight deficiency in the requirements may be of grave consequence. The severe cases of atrophy are usually due to a hydrolabile disposition, as they often show a tendency to diarrhea because of nutritive or carbohydrate deficiency; (3) Irritation diarrheas. In the vast majority of cases irritation diarrhea is brought about by an infection of the colon and ileum. These conditions resemble the catarrh of the air passages. They develop in proportion to the amount of immunity and resistance that is present. In an organ weak in its power of resistance bacteria become pathogenic; while in a healthy organ they are almost harmless. These three groups of diarrhea cannot be sharply distinguished as they may be associated with one another in various ways. In each case we have to deal with secondary inflammation of the intestinal tract.

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[13] Giffen, S. D.: The Feeding of Infants Based on Recent Experience, Ohio State M. J. **18**:829 (Dec. 1) 1922.

[14] Cowie, D. M.: A Simple, Practical Method for the Feeding of Infants. J. Michigan M. Soc. **22**:10 (Jan.) 1923.

[15] Hoobler, B. R.: Feeding of Infants and Children, J. Mich. M. S. **22**:16 (Jan.) 1923.

[16] Mucklow, A. E.: Infant Feeding, New York M. J. **117**:283 (March 7) 1923.

[17] Mixsell, H. R.: Some Newer Methods of Infant Feeding, J. M. Soc. New Jersey **20**:122 (April) 1923.

[18] Schmalfuss, M.: The Technic and Objects of Mixed Milk Feedings. Monatschr. f. Kinderh. **26**:387 (July) 1923.

[19] Finkelstein: On the Pathology and Therapy of Nutritional Disorders of Artificially Fed Infants, Yearly Courses for Physicians, Berlin, **1,** No. 6, June 1923.

Horwitt,[20] following the program of the German school, believes that their figures are the normal requirements for healthy infants. One-tenth of the body weight in milk and one-hundredth of the body weight in sugar or carbohydrate. He objects to the name of caloric feeding, yet he works out his feeding program on the basis of 45 calories for each pound, and where there has been undernourishment he has given as many as from 50 to 60 calories.

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[20] 20. Horwitt, S.: Theory and Practice of Artificial Infant Feeding, New York M. J. **117**:278 (March 7) 1923.

BUTTER FLOUR MIXTURES

All over Europe where there has been a deficiency of milk, the Czerny-Kleinschmidt butter flour feeding has gained in popularity. Articles by Gismondi,[21] Lecoq,[22] Ernberg,[23] Lowenburg,[24] Hamburger,[25] Schwartz,[26] Kasteele,[27] Poulsen[28] and Becking[29] describe the usual method of preparing butter flour, as laid down by Czerny-Kleinschmidt in their article in 1918.

Lowenburg[24] feels that fat feeding is sometimes a great problem. To find a way of supplying this food in sufficient amount and in acceptable form for the digestive apparatus, he has tried to ascertain why it is possible to feed large amounts fat in the butter flour mixture, when the same amount of cream or top milk added to a formula could not be tolerated. There seems to be some advantage in the use of boiled butter over raw butter and cream. The presence of flour or starch seems to insure an even distribution of the fats. Hamburger[25] mentions the use of complementary flour feedings in healthy breast fed children and gives his results. For healthy artificially fed children he substitutes butter flour mixtures for some of the carbohydrate gruels, used to dilute the milk, without changing the rest of the diet. The whole amount of butter is 5 per cent., combined with 5 per cent. flour. In cases of atrophy and dyspepsia he uses one-half buttermilk with varying amounts of sugar, to which 50 gm. of butter-flour porridge is added. He has noted in the new-born and premature baby an intolerance to this form of fat. Poulsen[28] has presented a report on his experience with the use of butter-flour feeding in children under one year. He prepared his

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21. Gismondi: The Butter-Flour Food of Czerny and Kleinschmdit in the Feeding of Infants, Riv. di clin. pediat. **20:**577 (Oct.) 1922.

22. Lecoq: Lactated and Other Flours and Meals Employed for Artificial Feeding, Soc. Sc. d'hgy. aliment. **10:**552 (Nov.) 1922.

23. Ernberg: Experiences with a Butter-Flour Dietary, Acta pediat. **2:**149 (Dec. 16) 1922.

24. Lowenburg, H.: A Comparative Chemical and Clinical Study of Boiled Butter and Cream in Infant Feeding, New York M. J. **117:**295 (March 25) 1923.

25. Hamburger, R.: Further Experiments with Butter-Flour Feedings, Monatschr. f. Kinderh. **25:**254 (March 25) 1923.

26. Schwartz, A. B.: The Present Status of Infant Feeding with the Butter-Flour Mixture of Czerny-Kleinschmidt, Wisconsin M. J. **21:**539 (May) 1923.

27. Kasteele: Experiences with Butter-Flour Feedings in the Milk Station of the Fishing Hamlet of Schevenignen, Monatschr. f. Kinderh. **25:**314 (March 25) 1923.

28. Poulsen, V.: Experiences wtih the Czerny-Kleinschmidt Butter-Flour Feedings, Monatschr. f. Kinderh. **25:**539 (March 25) 1923.

29. Becking: Results with the Czerny-Kleinschmidt Butter-Flour Feeding at the Utrecht Pediatric Clinic. Nederl. Maandschr. v. Geneesk. **12:**1 (July) 1923.

mixture according to the original formula of Czerny-Kleinschmidt.[30] He gives as much as from 200 to 250 gm. per kilogram of body weight each day. Forty-three cases showed a weekly gain of from 200 to 300 gm. In no instance was the butter-flour diet continued for more than three months. The child could then be discharged from the hospital as it had become accustomed to a normal diet.

In studying the literature on the use of butter-flour feeding, one cannot help but feel that in America the necessity for the use of this preparation is not as urgent as in Germany. The average good milk in America contains 4 per cent. fat, while in Germany the milk contains between 1 and 2 per cent. The addition of butter then becomes a necessity.

ACIDIFIED MILK

Nuller [31] studied the buffer value of cow's milk, both full milk and whey, on the basis of accurate electrometric titration curves. Cow's milk proved to be especially well buffered at from p_{H} 6 to 4.5. The buffering action of whey albumin is extremely slight. Casein, on the other hand, has an extensive buffering action which causes the strong buffering of cow's milk in the p_{H} region of from 6 to 4. The different position of hydrogen-ion concentration on milk feeding and on meat diet is explained by the different buffering capacity of the gastric juice which is produced. The buffering of the milk predominates in the gastric needs of infants. Babbott [32] made 227 observations on the hydrogen-ion concentration of the gastric contents in forty-three infants, from 3 to 19 months of age. For the test meal a powdered milk preparation, dissolved in distilled water, was used because its composition remained constant and its concentration could be varied at will. The composition of this mixture was fat 12 per cent., lactose 46 per cent., protein 32 per cent., salt 7 per cent. and moisture 3 per cent. A formula of 8 parts powdered milk to 100 parts water was given because it corresponded approximately to skimmed milk. The hydrogen-ion concentration of this meal was determined colorimetrically as 6.2. The normal range of hydrogen-ion concentration of the gastric contents on the milk test meal at the end of one hour was from p_{H} 3 to 2.5 with 76 per cent. of the readings between p_{H} 3.9 and 4.6. Acid production and hydrogen-ion concentration increases with increase of age. The greater the gastric acidity the more rapidly the stomach empties. The secretory capacity of infants is limited, so that when larger amounts of food are given they are no longer able to reach the optimal acidity.

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[30] Czerny-Kleinschmidt: Butter-Flour Feeding, Jahrb. f. Kinderh. 1918.

[31] Nuller: The Buffer Capacity of Cow's Milk. Ztschr. f. Kinderh. **35**:285 (June 7) 1923.

[32] Babbott, F. L.; Johnston, J. A.; Haskins, C. H., and Shohl, A. T.: Hydrogen-Ion Concentration of Gastric Contents of Infants, Am. J. Dis. Child. **26**:475 (Nov.) 1923.

Rosenbaum [33] has tried to determine whether the addition of hydrochloric acid causes more rapid emptying of the stomach. He finds that protein catabolism does not occur after mere addition of hydrochloric acid, up to the usual degree of acidity in preliminary peptic digestion. The excess of buffer value in cow's milk delays, in many cases, the gastric digestion in infancy by inhibiting the necessary acidity for the efficiency of gastric enzymes. To overcome this deficiency Faber [34] has suggested modifying cow's milk by addition of 0.4 per cent. hydrochloric acid. For this modification 20 c.c. of acid is added to each 100 c.c. of milk and the preparation called 25 per cent. hydrochloric acid milk. This milk, with its reaction of p_H 6, is slightly acid; it is ingested by infants without the slightest protest. The acid is taken up largely by the basic phosphates and corresponding chlorids. The increase in soluble calcium salts may be an additional advantage. No free acid is present in the milk, yet there is sufficient acidity to inhibit the growth of bacteria. In his experience the effect of this milk is to produce lime soap stools, like those from protein milk and to affect favorably the transition of fats, but it does not influence the digestion of sugars. Usually the transition from hydrochloric acid milk to an ordinary milk formula is easy. He does not believe that acidified milk should be given to infants during the first 6 weeks of life.

In studying the acidity of the gastric contents in infants, Marriott [35] examined forty-one normal infants under 1 year of age. Twenty-three infants were breast fed and seventeen received breast milk from the bottle. The average hydrogen-ion concentration of the gastric contents for the whole series was 3.75. In a group of sixteen infants, most of them extremely undernourished, including cases of infection (otitis media, pneumonia, dysentery), the gastric contents showed a hydrogen-ion concentration of from 4.4 to 4.8; the average being 4.74. In order to overcome the high buffer value of sweet cow's milk, which neutralizes a considerable portion of the acid of the gastric juice, the addition of one teaspoonful of lactic acid (U. S. P. from 75 to 85 per cent.) to each pint of milk is necessary. This is a sufficient amount to bring the acidity of the gastric contents approximately up to normal. Besides the important effect of increasing the acidity of the gastric contents it has an antiseptic action. It also stimulates the flow of bile, pancreatic juice, and intestinal secretion. Marriott[36] has combined the use of corn syrup with the lactic acid milk mixture with very gratifying results. Corn syrup is used in the same proportion as granulated sugar, 120 calories for each ounce. Dohnal[37] has examined the acidity of the gastric juice when from 50 to 100 gm. buttermilk were given after from one to three breast feedings. Forty-five minutes after the feeding the free and combined hydrochloric acids were estimated. Later, the actual amount of hydrochloric acid was determined by Barun's ash method. Tables show that there were daily and hourly variations in acidity valuation. After buttermilk there were high degrees of acidity, which were as large as the amounts of acid introduced into the stomach. In prematurely born children the favorable effect of buttermilk seems to be partly due to hydrochloric acid excretion. The result of his examinations showed that the acidity of the gastric juice in infants is variable, while the hydrochloric acid concentration is constant. The hydrochloric acid is increased by buttermilk. These facts indicate the advantage of giving buttermilk.

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[33] Rosenbaum, E.: Gastric Secretion in Infants, Monatschr. f. Kinderh. **24**:487 (Jan.-Feb.) 1923.

[34] Faber, H. K.: Hydrochloric Acid Milk in Infant Feeding, Am. J. Dis. Child. **26**:401 (Nov.) 1923.

[35] Marriott, W. McK., and Davidson, L. T.: The Acidity of the Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

GOAT'S MILK

Brouwer,[38] quoting the work of Schemtema, noticed that many children fed on goat's milk suffered from severe anemia, which was frequently accompanied by great enlargement of the spleen and sometimes enlargement of the liver. He reports five patients, aged 9, 9, 12½, 8 years, and 5 months. Breast milk was either not given or given for too short a time. The goat's milk was diluted one-half with water, adding a moderate amount of flour and sugar. All the children had loss of appetite, vomiting, and diarrhea. Their skin was pale and slightly yellow, with changes in the bony structure similar to rickets, and they were underweight. The blood picture resembled that of von Jaksch's anemia. The leukocyte count was high, reaching 70,000; the percentage of polymorphonuclear leukocytes was small, with myelocytes always present. Czerny-Kleinschmidt thinks that one-sided feeding with milk is an etiologic factor in von Jaksch's anemia. In order to confirm the alimentary character of the anemia they treated the gastrointestinal disturbance with albumin milk and then buttermilk. The children recovered rapidly. This anemia did not occur when breast milk was given with goat's milk, but where goat's milk was given early when breast milk could no longer be had, the anemia occurred in every case. In thirty-nine cases of severe and moderately severe anemia, in children

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36. Marriott, W. McK., and Davidson, L. T.: Acidified Whole Milk as a Routine Infant Food, J. A. M. A. **81**:2007 (Dec. 15) 1923.

37. Dohnal, E.: The Action of Buttermilk on Stomach Secretion, Monatschr. f. Kinderh. **27**:58 (Oct.) 1923.

38. Brouwer, E.: Goat's Milk Anemia and Goat's Milk Feedings, Jahrb. f. Kinderh. **102**:257 (July) 1923.

under 2 years of age, it was definitely stated that twenty had been fed with goat's milk; most of the children were less than 1 year of age. From 1914 to the end of 1920 goat's milk was the most frequent cause of anemia in children. Goat's milk anemia is a mild blood disease, but, in spite of this, deaths have occurred. In young infants breast milk naturally deserves the preference. After recovery from the gastro-intestinal disturbance, fruit juices, vegetables and cereals can be given. Frequent examination of the blood picture is necessary. In very severe cases blood transfusion should be tried.

THICK CEREAL FEEDING

In his three years' experience with the use of thick cereal feeding Mixsell[39] reports some splendid results. His indications for the use of this preparation are: (1) malnutrition (marasmus), (2) pylorospasm (mild or severe), (3) pyloric stenosis, (4) breast fed colic cases, (5) persistent vomiting (neuropathic), (6) idiosyncrasy for breast or cow's milk, (7) liquid food intolerance, (8) acute gastritis with vomiting, (9) eczema and allied skin conditions, (10) acute ileocoloitis with vomiting, (11) prematurity with defective assimilation, and (12) acute infectious fevers. The stock formula is made as follows: One level tablespoonful of farina to from 5 to 6 ounces 1 per cent. skimmed milk. In very young or premature infants the skimmed milk may be diluted with water half and half. One level tablespoonful of cane sugar or dextrimaltose to 30 ounces of mixture. This cooked together from 30 to 60 minutes, using either a single or double boiler, until the resulting mixture is so thick and tenacious that it will barely fall off an inverted spoon. Thorough cooking is absolutely essential. There is usually some difficulty in getting the baby to take its feedings when first put on thick cereal. This difficulty is overcome by using larger amounts of cane sugar, which makes it more palatable. From 70 to 80 calories for each pound of body weight is divided up among the required number of feedings for the child's age. Each ounce of the mixture contains 24 calories. From 3 to 4 hour intervals may be employed for feeding.

METABOLISM STUDIES ON INFANT GROWTH

Rost[40] studied the effect of the addition of calcium to the food of fifty children. To undertake this study he prepared cakes containing a known quantity of calcium. In order not to increase the food and calories suddenly, two calcium free cakes were given for a seven weeks'

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39. Mixsell, H. R.: Three Years' Experience with Cereal Feedings in Infancy in Malnutrition and Allied Conditions, Atlantic M. J. **26**:744 (Aug.) 1923.

40. Rost: The Nutritional Condition of the Children of the Berlin Orphans' Home with Special Consideration of Calcium Metabolism, Arch. f. Kinderh. **72**:81 (Nov. 18) 1922.

preliminary period. Then calcium cakes were given for seven weeks; calcium lactate being used. Two cakes contained a total of 80 gm. These were made up of wheat flour, corn meal, margarine, sugar and spices. Analysis showed sodium 1.04 gm., calcium monoxid 0.035 gm., calcium magnesia 0.074 gm., and fat 7.36 gm. The caloric value was 352. The children were in a good state of nutrition, being only slightly below normal in height and weight as a result of their war experience. After a continuous diet for six weeks, with a daily allowance of 3.6 gm. calcium lactate, corresponding to calcium monoxid 0.77 gm., two tests were made at the beginning and at the end of the calcium period, with considerable retention of calcium.

In taking up this question from a slightly different point of view, Holt [41] investigated the calcium metabolism of seven healthy children between the ages of from 2 to 6 years, first, on the usual hospital diet of whole milk, cereal, bread with butter, meat or eggs, fresh vegetables, potato or rice, and stewed fruit, and later on a reduced fat intake. It was possible to reduce the fat by substituting fat free milk for whole milk, increasing the bread, cereal, fruit, and adding cane sugar. During the fourth day preliminary metabolism period, on a mixed diet, the calcium was normal. The absorption was 0.51 gm. daily or 0.028 for each kilogram. This was very close to the average found by others for healthy children of the same age. Fat absorption was normal and fat excretion in the usual amount and form, as soap, fatty acids and neutral fats. After one week on low fat diet, the total daily amount of solids in the stools had increased from 16.8 to 24.4 gm., after three weeks it was averaging 34.3 gm. daily. Calcium oxid excretion after one week had increased from 1.34 to 1.81 gm. and in three weeks it had increased to 2.22 gm. This was more than the intake or a negative daily calcium oxid balance. In summarizing his observations Holt [41] observed that the stools uniformly change from a smooth, normal alkaline consistency, well digested, to one acid and foul, with an excess of fermentation and undigested food residues. Whether this change was due to the reduction of fat or to increased carbohydrates, or to both factors, it is impossible to say definitely. The increase in calcium oxid excretion was in most cases due partly to the fact that on a low fat diet the daily amount of total solids in the stool was markedly increased. The calcium oxid percentage of total solids in the stool was high. From his observations, the indications are that a low fat diet diminishes calcium oxid absorption. Whether this is dependent on a definite relationship between the fat and calcium in the diet, or whether

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41. Holt, L. E., and Fales, H. L.: Calcium Absorption in Children on a Diet Low in Fat, Am. J. Dis. Child. **25**:247 (March) 1923.

the fat intake influences calcium oxid absorption, chiefly by the maintenance of a proper condition, it is impossible to say.

In studying basal metabolism and its influence on growth in young children, Fleming[42] has plotted two curves. These show the yearly increase in weight of a normal child per kilogram, for the first 10 years of life; also the daily basal metabolism per kilogram. These two curves do not correspond very closely, except in the first 2 years of life, they both show the same tendency to flatten out as the age increases and the rate of growth decreases. They apparently afford a certain amount of evidence in favor of high basal metabolism in the growing child, which may be accounted for by the amount of energy expended in the manufacture of new tissue. Quoting the work of Rubner[43] he places the figure of the growing human being at 5.2 per cent. of the calories in the diet, as retained in the form of new tissue; on an average of 27 calories daily during the first half year of life. Calculations have not been published to show how much of the basal heat output is devoted to the manufacture of new tissue.

In investigating the relationship of the course of enteral salt fever and the calcium content of the serum, Schoenfelt[44] believes there is still a great deal of dispute regarding enteral sodium chlorid fever. He believes this is due to a combined action of whey and sugar in the infant's intestine. For the experiments regarding the course of the fever and the chlorin curve, only infants without infections or serious nutritive disturbances were used. From his observations on salt fever he is inclined to make the interpretation that it is a direct elective action of the salt on the heat centers and of the nerve tracts leading to it. In a number of patients the administration of sodium chlorid produced all the symptoms of alimentary dyspepsia, evidently due to injury of the gastro-intestinal function. The irregular and uncharacteristic temperature elevation in these cases distinguishes it from true salt fever. There is a time connection between the fever curve and the blood chlorin curve, from which it is evident that if the salt acts directly to produce fever it must act through the blood. Also in patients in which there is no fever after the giving of salt there is a rapid rise in the blood chlorin curve. The absence of fever can then be explained only on the basis of other factors or complications.

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42. Fleming, G. B.: The Influence of Growth on the Basal Metabolism of Children, Am. J. Dis. Child. **25**:85 (Feb.) 1923.

43. Rubner: Das Problem der Lebensdauer und Seiner Beziehung zu Wachstum und Ernahrung, Ztschr. f. Biol. **36**:1, 1898.

44. Schoenfelt: Theory of Enteral Salt Fever, Experiments on the Relation Between the Course of the Fever and the Calcium Content of the Serum Arch. f. Kinderh. **72**:120 (Nov. 18) 1922.

ANTISCORBUTIC CAPACITY OF DIFFERENT FOOD SUBSTANCES

Lesne[45] has tested guinea-pigs with various milk preparations. Milk boiled for ten minutes produced no scorbutics. A year old, unsweetened, condensed milk sterilized at high temperature produced scorbutus. Aging after sterilization clearly destroys the vitamins. A similar preparation recently sterilized kills the test animal by producing scorbutus. More than 50 per cent. of infantile scurvy is caused by milk that has been rendered homogeneous. Saccharose or lactose is antiscorbutic. Test animals fed with powdered milk die of scurvy in the same time as those fed with sterilized milk. Very few of the prepared milks are capable of protecting infants or guinea-pigs against scurvy. Some infants resist the absence of vitamin remarkably. Orange, lemon or tomato juice should be employed in artificial feeding. Lemaire[46] described the development of scurvy in an infant, aged 9 months, fed on fresh cow's milk. The milk was sent from a farm not far distant; it was subjected to a single heating for ten minutes, before being placed in the nursing bottle, but not modified in any other way. Cure was readily obtained with lemon juice. He called attention to the fact that this disease is relatively not infrequent, even though milk is heated twice or more. Leichtentritt,[47] in a clinical experiment on this subject, has tried to determine the effect of certain substances on lemon juice. Lemon juice boiled for one hour does not interfere with growth. Exposing lemon juice to ultraviolet rays or passing oxygen through it does not change its effect. When it is allowed to stand for several days the antiscorbutic action is lessened.

OTHER TYPES OF FOOD USED IN INFANT FEEDING

McIlwaine[48] advocates the use of dried milk as one of the weapons with which to combat digestive disturbances in infants, or to tide over a critical period. Properly prepared it is sterile and will keep indefinitely. It is not easily contaminated even by the most ignorant. In traveling it is a great help, as its preparation is so simple. He takes exception to the French idea that if milk powders are kept too long scurvy may result. He has found, on the contrary, that they may be used after several months or even a year's time. Chemically, they are not comparable to fresh milk, although they are very superior to a good many specimens of fresh cow's milk. In an analysis of fifty cases he shows some very good results. Dryco was the milk powder employed.

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[45] Lesne, E.: Antiscorbutic Capacity of Different Milks Employed for Infant Feeding, Nourrisson, Par. **10**:377 (Nov.) 1922.

[46] Lemaire, H.: Barlow's Disease in an Infant Fed on Fresh Cow's Milk, Bull. Soc. de pédiat. de Par. **7**:329 (Oct. 17) 1922.

[47] Leichtentritt, B.: Clinical and Experimental Studies on Barlow's Disease, Ztschr. f. d. ges. exper. Med. **29**:658 (Oct. 18) 1922.

[48] McIlwaine, M. N.: Virginia M. Monthly **49**:700 (March) 1923.

Muller[49] has described the use of potato flour in feeding young children. This has been brought about by the restriction of fresh food in Berlin; the population was required to use potato flour and other forms of starch. Ordinary potato flour, being pure starch, should not be employed. This can be overcome by roasting the flour, which partly converts the starch. The vitamin content of potatoes is not large, so that it suffers still further in the drying of the potatoes and the roasting of the flour. It is higher, however, than the vitamin content of other flours recommended for child feeding. There are no digestive disturbances on changing to this flour. The slightly laxative action is often an advantage. The stools are somewhat more solid than when wheat flour is employed. The urine shows a leaning toward the alkaline side, while in most infants flours convert the reaction to an acid one. According to current theory potato flour is indicated in rickets and contraindicated in tetany.

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[49] Muller, E.: Potato Flour in the Feeding of the Small Child, Klin. Wchnschr. **1**:2378 (Nov. 25) 1922.

News and Comment

The French Association of Pediatrists will hold its fourth Congress for French speaking Pediatricians, September 29, 30 and October 1, 1924, at Paris, under the presidency of Dr. Marfan. The following questions are to be reported on:

First: Etiology and Pathogenesis of Rickets, by Lesné.

Second: Prophylaxis and Treatment of Syphilis in Childhood, by L. Tixier.

Third: The Treatment of Empyema in Childhood, by Ribadeau-Dumas and Rocher.

Abstracts from Current Literature

Anatomy and Physiology

Further Observations Upon the Shadows of the Thymus and the Heart. L. R. DeBuys and E. C. Samuels, South. M. J. **17**:260, 1924.

Four hundred and fifty observations were made on newly born infants and infants aged 6 months and 1 year. All the observations were true anteroposterior exposures. The study shows that the heart apparently does not rotate during the first year as the individual grows, but the shape remains the same as to type and position. There is an increase in its size. The great blood vessels of the mediastinum show a decided lengthening during the first year period.

The growth of the size of the heart is not influenced by the size or position of the thymus.

The shadow of the thymus does not gradually increase or decrease uniformly in the healthy infant within the first year of life. It may vary in size in the same person at different periods within the first year. The variations in the size of the shadows may exist without clinical evidence of disease.

Schlutz, Minneapolis.

Relation of Flexors to Extensors in New-Born. C. Ritter, Jahrb. f. Kinderh. **104**:*293*, 1924.

So far as weight is concerned, the relation of flexors and extensors of the extremities is practically the same in infants and adults. The flexion of the extremities in new-born infants, therefore, is not due to greater development of flexors. It is more likely that reflex nervous relationships are the cause.

Sutherland, Chicago.

Pathology and Bacteriology

The Intradermal Salt Solution Test. II. Its Prognostic Value in "Nephritis" with Generalized Edema. C. A. Aldrich and William B. McClure, J. A. M. A. **82**:1425 (May 3) 1924.

It was found that the elevation produced by the injection of 0.2 c.c. of 0.8 per cent. sodium chlorid solution disappeared in normal children of 1 year of age, or over, in sixty minutes or longer.

Since the disappearance time sharply decreases coincident with or preceding the development of edema, and increases with or before the subsidence of edema, the curve of the disappearance time has been used as an index of the tendency to increasing or decreasing edema and as a means of ascertaining a return to normal.

The report of five cases substantiates the interpretation of the disappearance time curves. The observations made seem to confirm the theory that the tissues take an active part in the production of edema.

Henn, Chicago.

Histological Studies on the Iron Metabolism in Early Infancy. P. Schwartz, R. Baer and J. Weiser, Ztschr. f. Kinderh. **37**:167, 1924.

One hundred and fifteen infants were examined at necropsy and histologic studies were made of the livers and spleens. One group of thirty-eight consisted of stillborn infants and infants under 3 days of age. Ten per cent. of these infants were entirely free from iron in both liver and spleen as demonstrated by tissue stains. The remainder showed traces of iron in both organs. In the older infants increasing amounts of iron were found. This increase was found first in the periportal, endothelial tissues and in the red pulp of the spleen; later the iron was more generally distributed. The iron content of the liver and spleen ran parallel. The Küpffer cells appear several days after birth. At from four to ten weeks the liver and spleen show the maximal amounts of iron. After five months there is a gradual decrease of iron and at eight months or earlier both organs are again iron free.

ORGANIC ACIDOSIS IN INORGANIC ACIDOSIS, AND ALKALOSIS. H. BEUMER and ANNA SOECKNICK, Ztschr. f. Kinderh. **37**:236, 1924.

In acidosis following starvation, sodium bicarbonate and secondary sodium phosphate hastened the acetonuria; ammonium chlorid delayed it. The explanation of the action of these salts may be found in their effect on glycogen mobilization in the liver. Alkalosis favors the appearance of acetonuria in tetany, pneumonia, and lye poisoning.

THE ENDOTHELIAL SYMPTOM IN INFANTS. CLARA BEINTKER, Ztschr. f. Kinderh. **37**:225, 1924.

The Rumpel-Leede phenomenon was studied in 400 infants under 1 year of age and 100 children between 2 and 3 years of age. The tourniquet was kept on the arm from four to five minutes. The reaction (intracutaneous capillary hemorrhage) occurred in the first three minutes. In the 400 infants the phenomenon was positive in 36 per cent., in the 100 older children it was positive in 44 per cent. In the first three months the reaction was seldom seen. The phenomenon was observed in seven of ten cases of measles, in eight of twenty-three cases of pertussis, in 65.2 per cent. of twenty-three infants with syphilis, in 61.5 per cent. of thirteen tuberculous children, in 70 per cent. of twenty-four children with spasmophilia, and in 82 per cent. of fifty-six children with exudative diathesis. Two factors play a rôle in this endothelial symptom: (1) Constitutional diathesis; (2) nutrition.

PETERMAN, Rochester, Minn.

HAEMOLYTIC AND AGGLUTINATIVE PROPERTIES OF DIPHTHERIA ANTITOXIN (Preliminary Report). HOWARD OSGOOD, Bull. Buffalo Gen. Hosp. **2**:22, 1924.

Osgood believes that the reactions following the use of New York State Antitoxin intravenously, were not due to "tricresol laking." The presence of blood serum in great excess, he thinks, caused an inhibition of the laking. In his laboratory experiments, he also found slight agglutination of human erythrocytes by diphtheria antitoxin in 1:4 dilution.

This weak agglutinative activity, he thinks, would have no effect on the patient's erythrocytes when the antitoxin is injected intravenously.

FOUR CASES OF CONGENITAL DIAPHGRAGMATIC HERNIA IN THE NEW-BORN. W. F. JACOBS, Bull. Buffalo Gen. Hosp. **2**:26, 1924.

Jacobs adds four more cases of congenital diaphragmatic hernia to the series of 600 cases recently reported by Eppinger. He reports one case of aplasia of the esophagus, which is extremely rare.

A CASE OF OPEN MECKEL'S DIVERTICULUM WITH PROTRUSION OF EVERTED BOWEL THROUGH THE UMBILICAL CORD IN THE FORM OF A HERNIA SAC FILLED WITH LOOPS OF INTESTINE. THEW WRIGHT, Bull. Buffalo Gen. Hosp. **2**:30, 1924.

Wright reports an uncommon congenital condition due to faulty closure of the vitello-intestinal duct.

BACON, Chicago.

THE USE OF RABBITS FOR INTRACUTANEOUS VIRULENCE TESTS OF B. DIPHTHERIAE OR TITRATION OF DIPHTHERIA ANTITOXIN. D. T. FRASER and H. E. WIGHAM, J. A. M. A. **82**:1114 (April 5) 1924.

Rabbits of 2 kg., or more, in weight, with unpigmented skin are used; the back and flanks are clipped closely; this area is covered lightly with a thin paste of barium sulphid and starch 1:4; quickly and thoroughly washed off with soap and water, immersed in warm 0.85 per cent. saline solution and dried. The animals are prepared twelve hours before the test. Areas of approximately 3 by 3 cm. are outlined with a moistened indelible pencil. The injections of 0.1 c.c. are made with a 26 gage, short bevel needle, and syringe graduated in fiftieths of a cubic centimeter.

The skin reactions are comparable with those obtained in the skin of guinea-pigs. In rabbits, however, the areas are greater in extent and develop more slowly; necrosis, when present, is more superficial. The maximum reaction appears as a rule on the third day or even later. The minimal lethal dose of the toxin used in the authors experiments was found to be 0.005 c.c. for 250 gm. guinea-pigs; the L + dose of 0.38 c.c. contained seventy-six minimal lethal doses. One fifteen hundredth of the minimal lethal dose contained in 0.1 c.c. produces a very definite redness with scaling on the fourth day.

HENN, Chicago.

PREPARATION OF DRY ANTITOXIN AND AGGLUTININ POWDERS. EDWIN F. HIRSCH, J. Infect. Dis. **34**:390 (April) 1924.

Methods involving the hydrogen-ion control for the preparation of dry antitoxin and agglutinin powders are described. Dry powders of the antitoxins, in all probability, may be prepared from specific immune serums according to the method outlined.

The dry powder, with active agglutinating properties was prepared from rabbit and human plasma. It is a protein-acid salt, readily soluble in water, and in solution actively potent.

Agglutination has been obtained with mixtures of homologous bacteria in dilutions containing as little as 0.0035 mg. and 0.0022 mg. of dry weight per cubic centimeter.

One of the preparations has been stored about five weeks without loss of potency.

KENNEDY, Rochester, Minn.

EXPERIMENTS ON THE SURVIVAL OF THE FEBRILE HERPETIC AND ALLIED VIRUSES IN VITRO. JAMES E. MCCARTNEY, J. Exper. Med. **39**:533, 1924.

The author studied the survival and multiplication of the so-called virus of epidemic encephalitis and the virus of febrile herpes in artificial cultures. His experiments fail to confirm the statements previously made by Bradford, Bashford, and Wilson, by Loewe and Strauss, and by Thalhimer, that micro-organisms of the class of the globoid bodies of poliomyelitis may be cultivated by the use of the Smith-Noguchi anaerobic tissue method from the so-called virus of encephalitis lethargica. The experiments show equally that the herpes virus does not multiply in this medium. They indicate, moreover, that the medium is unfavorable to the survival of the virus, while ordinary broth under aerobic conditions is more favorable for maintaining the activity of both of the viruses.

It has also been shown that the viruses can be passed from brain to brain in the rabbit through a long series, without contamination with cocci or other common bacterial forms. Hence the author regards all reports of the finding of ordinary bacteria in the brain of cases of epidemic or lethargic encephalitis as instances of mixed or secondary infection arising during life, or examples of necropsy invasion of the body, or a faulty technic at necropsy.

Experimental Human Inoculations with Filtered Nasal Secretions from Acute Coryza. Robert C. Robertson and Robert L. Groves, J. Infect. Dis. **34**:400 (April) 1924.

The nasal secretions of eleven patients suffering with acute coryza were collected, diluted with normal salt solution and filtered through a Berkfeld filter. Cultures were made from each filtrate. All cultures were negative after ninety-six hours aerobic and anerobic incubation. On smears made from the filtrates, coccoid bodies were found.

Spraying the filtrates on the nasal mucosa of one hundred healthy persons was followed, for a period of twelve days, by upper respiratory or bronchial affections in only five cases. These cases were considered due to causes other than the inoculations.

During an acute attack of coryza, definite variations were noted in the bacterial flora of the secretions. During the onset and early stages of the attack, there was a marked diminution of the total bacterial flora, with an equally marked predominance of one of the normal habitants—usually staphylococcus albus.

During the purulent stage of the attack, a marked increase of all organisms over the normal flora of health was observed although the predominance of one organism still remained. The later stages of the attack were marked by a gradual return to the normal flora of health.

Kennedy, Rochester, Minn.

The Effect of Digestive Juices on the Potency of Botulinus Toxin. Jacques J. Bronfenbrenner and J. Monroe Schlesinger, J. Exper. Med. **39**:509, 1924.

Botulinus toxin is a notable exception to the general rule that true toxins from cultures of pathogenic micro-organisms tend to be harmless when taken by mouth. The marked toxicity of botulinus toxin when ingested brings up the question of its path of absorption and its resistance to gastric and intestinal secretions. Landman found that it resisted exposure to fifth normal hydrochloric acid solution for twenty-four hours, but neither he nor other earlier investigators took into account the buffer content of the vehicle fluid in which the toxin is present.

The authors investigated the effect of changes of hydrogen-ion concentration (to which the toxin is subject in passing through the stomach and intestines) either alone or combined with the effect of the digestive ferments. The potency of the toxin was tested by intraperitoneal injection into mice. They conclude that botulinus toxin resists a degree of acidity equivalent to that of the stomach, even when exposed thereto for twenty-four hours at 37 C. In a medium of weakly alkaline reaction, however, its potency is reduced to less than one-tenth in twenty-four hours. It is unaffected by peptic and tryptic digestion. Because of its instability in mildly alkaline solutions and resistance to acids, there is reason to believe that the toxin is in the main absorbed from the upper portion of the digestive tract, i. e., the stomach and upper duodenum.

McClure, Evanston, Ill.

The Effect of Anesthesia and of Sedatives on the Serum Therapy of Experimental Botulism. Jaques J. Bronfenbrenner and Harry Weiss, J. Exper. Med. **39**:517, 1924.

The rapid progress of the intoxication in severe cases of botulinus poison in man has rendered of questionable value the therapeutic use of antitoxin in such instances. The time required for making the diagnosis and the delay in obtaining the antitoxin consequent on the few points of distribution, usually results in the use of the antitoxin too late. More numerous and widespread sources of supply of antitoxin are desirable. At the same time a procedure was sought to retard the progress of the intoxication sufficiently to allow more time for the effective administration of antitoxin. The effect of various anesthetics and sedatives was tried out in this respect on guinea-pigs. The authors found that when guinea-pigs are fed large amounts of botulinus toxin they develop symptoms of intoxication within six hours and die usually within twelve hours. Introduced intraperitoneally in large amounts the animal may show symptoms of intoxication at the end of the first hour and die usually within two hours.

If these animals are placed under anesthesia following theadministration of toxin, the intoxication proceeds much more slowly. Anesthesia, by ether, is effective whether the toxin is given by mouth or intraperitoneally. Life in the guinea-pigs kept under ether after the administration of lethal amounts of toxin is prolonged by a period approximately equal to that during which ether anesthesia is continued. When anesthesia is discontinued, the intoxication proceeds at its usual rate. Anesthesia delays the progress of intoxication not only when administered immediately after the intake of toxin, but when administered much later after the intoxication had progressed far enough to cause definite objective symptoms of poisoning. At this late stage of intoxication, the unsupported serum therapy of botulism in guinea-pigs usually remains without effect. If the animals are anesthetized at this time and kept under the influence of ether for some time, antitoxin therapy becomes effective. Indeed the antitoxin treatment can be delayed further for several hours, provided the animals are kept under anesthesia during the interval. Results of similar nature were obtained with luminal sodium, nitrous oxide-oxygen mixture, and morphin used in place of ether.

McClure, Evanston, Ill.

Experimental Poliomyelitis in Rabbits. Mary Nevin and Florence R. Bittman, J. Infect. Dis. **34**:420 (April) 1924.

A 5 per cent. unfiltered suspension of poliomyelitis virus, obtained from the Rockefeller Institute, was inoculated intracerebrally, intraperitoneally and intravenously, or by a combination of these methods, into young rabbits. Of the series of rabbits used, only one developed symptoms suggestive of the disease. The clinical condition of the rabbits and the examination of the central nervous system indicated that the effort to produce the disease by this means was unsuccessful.

Spontaneous Recovery of Rabbit from Experimental Rabies. Rigne D'Aunoy, J. Infect. Dis. **34**:425 (April) 1924.

A case of spontaneous recovery of a rabbit from rabies, after full development of symptoms following intracerebral injection of fixed dessicated virus, is reported. Saliva from this animal obtained sixteen days after inoculation, when injected intracerebrally into rabbits produced typical rabic symptoms with Negri bodies in brain sections. Forty days after inoculation the animal's saliva was no longer infectious. Blood serum secured seventeen and ninety days after injection showed no appreciable antirabicidal action.

Spontaneous Encephalitis in Rabbits. Ernest W. Goodpasture, J. Infect. Dis. **34**:428 (April) 1924.

Large gram-positive bacillary organisms have been demonstrated in the cerebral lesions of spontaneous encephalitis of rabbits. The cerebral lesions are vascular in distribution and are the manifestation in the brain of a generalized infection, which may produce similar lesions in the lungs and kidneys in which morphologically identical organisms have been found.

Streptococci in Relation to Etiology of Epidemic Encephalitis. Edward C. Rosenow, J. Infect. Dis. **34:**329 (April) 1924.

Rosenow reports the results obtained in an extensive study of the relation of streptococci to experimental encephalitis. Consistent results have been obtained in a series of undoubted cases of encephalitis, representing a wide range of types of the disease, and extending over a period of four years. Somewhat peculiar streptococci, much alike in the different cases, have been isolated constantly from infected tonsils, teeth or nasopharynx during life, and from the brain after death. With this streptococcus in freshly isolated cultures, after as high as forty-four rapidly made subcultures, and after a series of animal passages, characteristic symptoms and lesions of different forms of encephalitis have been reproduced in animals.

Peculiar neurotropic properties of the streptococcus have been noted in four species of animals, rabbit, monkey, mouse and guinea-pig, following various methods of inoculation. Intracerebral inoculation, the method that has been so successfully used in virus studies in poliomyelitis, has given the best results. Results such as in these experiments were not obtained with green-producing streptococci from sources other than encephalitis. The organism has been demonstrated in the lesions which develop spontaneously in man, and which have been produced experimentally in animals, and proved absent in adjacent normal tissues and in the brains of persons and animals that died from other causes. It has been shown to possess specific antigenic properties. Most of the strains are immunologically alike, as determined by agglutination experiments with hyperimmune serums. The serum of patients with acute forms of the diseases agglutinated specifically the homologous and many heterogeneous strains. The requirements for proof of the causal relationship between this streptococcus and encephalitis seem to have been fulfilled.

The organism varied greatly in size and shape, depending apparently on conditions of growth. Filtrates of nasopharyngeal washings, of emulsions of the brain in fatal cases, and of old anerobic cultures have often yielded the streptococcus in culture and in positive animals. Large and extremely small forms sometimes in the same chain, and large oval forms breaking into small forms have frequently been seen in cultures and have been demonstrated repeatedly in the lesions in undoubted cases of encephalitis.

Kennedy, Rochester, Minn.

Methods and Significance of Tests of Stomach Function. Fritz Müller, Monatschr. f. Kinderh. **27:**415, 1924.

All previous methods of stomach examination such as roentgen ray and even chemical examination of stomach contents are inexact, because the emptying time of the stomach and the acidity of the stomach contents are in close relationship.

Formerly, the acidity of the stomach contents was determined by titration, now the hydrogen-ion concentration is determined. A variety of test meals have also been suggested, but many of these do not consider the buffer action of the salts.

Müller illustrates this by the following experiment. He gave a mixture of milk and sodium hydroxid having a p_H of 10. After thirty minutes, 40 c.c. of secretion was removed with a p_H of 7.7. After one hundred and twenty minutes, 48 c.c. with considerable mucus, was removed with a p_H of 6.2.

In another experiment, he gave a mixture of milk and hydrochloric acid, the mixture having a p_H of 4.15. After thirty minutes, 3 c.c. of secretion was removed with a p_H of 4, after one hundred and twenty minutes, 13 c.c. of gastric juice was removed, having a p_H of 3.3.

On account of these observations Müller concludes that neither tea nor gruel should be used for test meals, for: (1) they exert unphysiologic irritation; (2) their emptying time is irregular; (3) the rapidly increasing acidity of the secretion may keep down the amount.

The most satisfactory test meal he has found is a mixture of equal parts skimmed milk and oatmeal gruel. Of this mixture, to a baby weighing 3,500 gm, he gives 120 c.c. For a baby weighing 5,000 gm., he gives 160 c.c., and for babies weighing over this he gives 200 c.c.

The stomach contents should be removed in one hour.

Basal Metabolism in Childhood. Fritz B. Talbot, Monatschr. f. Kinderh. **27**:465, 1924.

Benedict and his co-workers have been able to construct a respiratory chamber which permits the estimation of both carbon dioxid and oxygen. As this apparatus is practicable for experiments as short as one-half hour, much advance in the study of metabolism has been made. Technically speaking, basal metabolism requires the subject to be at absolute rest with the stomach empty. As this is impossible in infants, these subjects have been investigated during the quiet period following a feeding. Howland has proved that the indirect method is just about as accurate as the direct measuring of heat given off by the body.

That muscular activity increases basal metabolism has been investigated by Rubner and Heubner in 1898, and confirmed by Howland in 1912. Benedict and Talbot, in carefully controlled experiments, showed that metabolism was increased by muscular activity from 30 to 40 per cent., and in one very restless crying child by 211 per cent.

Benedict and Talbot, as well as Bailey and Murlin, confirm the original observations of Hesselbach that basal metabolism in the new-born is very low and increases proportionally to age. In a like manner, the respiratory quotient falls rapidly from birth to 0.73 on the third day, showing that the glycogen supply has been exhausted and that a large part of the body energy is supplied by the fat. In premature and the new-born infants a relation exists between heat production and body weight, the smaller the child the lower the heat production. However, the metabolism of the premature infant is probably greater than that of the fetus of the same weight, due to the demands of extra-uterine life. The metabolism of the premature infant is very slight in comparison to the normal infant.

In normal and older infants growth exerts a marked influence on metabolism. The curve of growth and heat production run nearly parallel for the first year, but after that, results are not definite.

Many observers agree that total heat production increases with age. The same relation applies to increase of weight, confirming Benedict and Talbot's theory that heat production depends on the active protoplasmic tissue of the body. This relationship is not so constant in girls, perhaps due to varying amounts of fat.

As regards the metabolism per kilogram of body weight with reference to age, this increases for the first year, and then gradually decreases. Fat children have lower metabolism than the thin ones.

Of children over 11 kg. in weight, girls have lower metabolism than boys, possibly due to their having less "active tissue" and more fat.

At puberty there is an increase, perhaps due to increased thyroid activity.

Food increases metabolism from 8 to 15 per cent. The latter is difficult to estimate in infants.

In disturbances of nutrition, the farther under the normal weight, the greater the child's metabolism, the baby probably using a larger proportion of body tissue for warmth.

The study of metabolism is of clinical value not only in feeding cases but in endocrine disturbances. It is markedly decreased in cretinism and can be used as a guide to the dosage of thyroid extract. The same applies to other types of thyroid disturbance. In mongolian idiocy no change was found. Studies have also been made on individual cases of dwarfs, congenital brain defects, dyspituitarism and amaurotic family idiocy.

Nutritional Disturbances

Concerning the Technic of the Use of Protein Milk. Paul, Monatschr. f. Kinderh. **27**:504, 1924.

It is now generally admitted that dyspeptic stools occur not only in cases of intestinal fermentation with acid bowel movements, but also with alkaline bowel movements, suggesting that the two processes, fermentation and putrefaction, go on simultaneously. As putrefaction in the intestine is associated with an increase of indican in the urine, Paul believes that the determination of the amount of indican in the urine would be an index of the predominance of fermentation or putrefaction in the intestine, and thus a guide as to the increase or decrease of carbohydrate.

Paul followed this procedure, and in those patients with stationary weight and indicanuria, in spite of dyspeptic stools, he increased the carbohydrate. These patients showed prompt response in the weight curve, the general condition improved and the bowel movements became normal.

Paul believes that this little test will prove a useful clinical guide to the dosage of carbohydrate.

Action and Effect of Hydrochloric Acid Milk in Tetany. R. Scheer and A. Salomon, Monatschr. f. Kinderh. **27**:406, 1924.

Scheer has previously reported the beneficial effect of hydrochloric acid on tetany, that is, he has shown that the influence of this acid causes disappearance of mechanical and electrical hyperexcitability. Many observers have disputed these conclusions with a suggestion that the syndrome may be due to a number of etiologic factors.

The authors determined to repeat their observations not only in clinical experiment, but also by determining the serum content of calcium and phosphate. Previously, Scheer had concluded that hydrochloric acid caused an increased phosphate excretion by the kidney.

The first experiments were made with a mixture of milk, 740 c.c., one-tenth normal hydrochloric acid, 260 c.c., 5 per cent. sugar. While many cases seemed to improve greatly under this mixture, a few of the very severe cases became worse. For the latter, they tried increasing the strength of the mixture to milk 600 c.c., tenth normal hydrochloric acid 400 c.c., giving a pH of from 3.5 to 4. Even the severely ill patients showed striking improvement on this mixture.

As regards the serum analyses, the phosphorus was decreased and the calcium increased.

This milk mixture seemed also of some value in cases where the bowel movements were very loose.

Gerstley, Chicago.

Scurvy in Childhood. B. Schagan, Jahrb. f. Kinderh. **104**:225, 1924.

In the years following the famine of 1918-1919, there was a great increase in cases of scurvy throughout Russia. Whereas in 1913 there were only 7.3 cases per 10,000 inhabitants in St. Petersburg, in 1920-1923, from 5.2 to 11.3 per cent. of the cases in the children's clinic were scurvy patients. The observations cover a series of 186 cases, 55 per cent. of which occurred in the spring and 32 per cent. in the summer. The highest incidence was in children from 2 to 8 years of age. The diet had a sufficient caloric content but was almost lacking in the antiscorbutic factor C.

Scurvy is a severe toxicosis with involvement of many organs, and a high mortality, 16 per cent., in the period studied. The stomatitis became gangrenous in 13 per cent. of the cases. The morphology of the blood and roentgen rays show a severe disease of the bone marrow. In this series 72 per cent. of the cases had a strongly positive Pirquet reaction, and 15 per cent. had a weakly positive reaction. This is taken to indicate that a latent tuberculosis is activated by scurvy. The general treatment, consisting of fresh vegetables and raw milk, gave good results, and the stomatitis was best treated locally with a 1 per cent. copper sulphate solution.

SUTHERLAND, Chicago.

NOTE OF THE CLINICAL SIGNS OF INFANTILE RICKETS AS OBSERVED IN VIENNA. H. P. WRIGHT, Canad. M. A. J. **14**:320 (April) 1924.

This article is a review of Part III, No. 3, special report series No. 27, of the Medical Research Council of Great Britain, 1923, by E. J. Dalywell and Helen M. M. Mackay.

The author concludes that craniotabes is practically always a sign of active rickets, and that it is an early sign.

The rachitic rosary is an important and early sign, but epiphyseal enlargement and delayed closing of fontanels are not considered of much importance in the early diagnosis. All other signs are considered variable. They divide rickets into two types: (1) rickets with low blood calcium and normal phosphorus and (2) rickets with low blood phosphorus and normal calcium.

MOORE, Omaha.

Diseases of the New-Born

CONGENITAL GOITER. H. H. SKINNER, J. A. M. A. **82**:1190 (April 12) 1924.

In twelve cases of congenital goiter, reported by Skinner, he believes that they are caused by iodin deficiency in the mother's diet. All grades of pathologic change may be seen, from a simple parenchymatous goiter with no symptoms, to marked enlargement with complete tracheal compression and cystic conditions causing serious danger to mother and child. Treatment is surgical for emergencies but mainly prophylactic by means of iodin administration to the mother.

LIGATION OF THE UMBILICAL CORD BEFORE THE CESSATION OF PULSATION. A. C. WILLIAMSON and J. V. TAYLOR, J. A. M. A. **82**:1107 (April 5) 1924.

The authors found that there was no appreciable difference in the weight or progress during the first 2 weeks in life, between babies whose umbilical cords were cut after cessation of pulsation and babies delivered by the cesarean method, whose cords were ligated immediately following delivery. Late ligation should not be urged on the ground that the infant thereby gains an extra appreciable amount of blood.

HENN, Chicago.

MENINGEAL HEMORRHAGES OF THE NEW-BORN. ALFRED GORDON, Am. J. Obst. & Gynecol. **7**:462, 1924.

The causes of meningeal hemorrhages are largely the result of tearing of the blood vessels in the cerebral membranes during labor. This is most marked in forceps and breech deliveries, especially if the delivery is terminated too rapidly or if the forceps are applied to the long diameters of the head. Due to the anatomy of the fixed point in the vein of Galen when the apex of the tentorium is drawn up, the tributary veins rupture. For this reason nearly half of the meningeal hemorrhages occur in the tentorium.

The author divides the hemorrhages into supratentorial and infratentorial. In the former, the blood cannot extend beyond the lower surface of the tentorium; in the latter, it may extend to the spinal canal. He advises spinal puncture in each case as a diagnostic procedure for localization of the lesion and treatment of the infratentorial. Early craniotomy in the supratentorial is directly indicated, and favorable results can be expected when the operation is performed within a few days after birth.

HEMATOCOLPOS IN A CHILD OF SIX WEEKS. G. L. MOENCH, Am. J. Obst. & Gynec. **7**:471, 1924.

The author reports a case of hematocolpos in a child, aged 6 weeks. The child was found dead in bed. There was no history of cough, fever, or illness.

Necropsy findings were normal except for the presence of a large patent foramen ovale, and some old tarry blood on the anterior parietal peritoneum which had evidently come from a small cyst of the right ovary. The hymen was imperforate and the vagina was dilated to the size of a golf ball by a collection of old blood. There was marked pulmonary edema, although the lungs were not fully expanded. The cervix was slightly eroded, but there was no evidence of a hemorrhagic diathesis. Probable diagnosis was either precocious menstruation or acute inflammation with hemorrhage.

ALLEN, Chicago.

Acute Infections

A SCARLET FEVER ANTITOXIN. GEORGE F. DICK and GLADYS HENRY DICK, J. A. M. A. **82**:1246 (April 19) 1924.

With the idea of producing a scarlet fever antitoxin, a horse was immunized by subcutaneous injections of sterile filtrate, from broth cultures of strains of streptococci that had produced experimental scarlet fever. Part of the horse serum was concentrated and tested in various dilutions. The tests revealed that the antitoxin had not been destroyed.

It will be necessary to determine the therapeutic value by the use of the antitoxin in a large series of carefully controlled cases.

THE RELATION OF THE DICK TEST TO SCARLET FEVER. C. F. BRANCH and F. G. EDWARDS, J. A. M. A. **82**:1260 (April 19) 1924.

Branch and Edwards, using streptococcus filtrate, made by the Dicks, found that: all convalescent scarlet fever patients tested gave negative reactions, that some patients ill with scarlet fever gave slightly positive reactions which became negative in the convalescent period two weeks later. The filtrate with which the Dicks produced 41.6 per cent. positive or strongly positive skin tests gave 40 per cent. positive tests in the hands of the authors. The control used was negative in all cases tested.

THE PROPHYLAXIS OF VARICELLA WITH CONVALESCENTS' SERUM. A. A. WEECH, J. A. M. A. **82**:1245 (April 19) 1924.

Nine infants exposed to varicella were given from 3.0 to 4.5 c.c. of convalescents' serum, intramuscularly, within from one to six days after exposure. Eight of them did not contract the disease. In the ninth infant an extremely mild attack developed after an unusually long incubation period of twenty-two days. The serum used was obtained from children in whom the disease had developed from ten to twenty days previously. Weech suggests the use of this serum in hospital practice, thus diminishing the period of quarantine.

FURTHER NOTES ON THE TREATMENT OF PERTUSSIS BY THE ROENTGEN RAY. H. I. BOWDITCH, J. A. M. A. **82**:1422 (May 3) 1924.

In three hundred cases of whooping cough treated by the roentgen ray, there was strong evidence that more than 80 per cent. were benefited by the treatment. Only one fatal case occurred. The most favorable results were obtained in the early stages of the disease and in the younger children.

The justification of the roentgen-ray therapy is based on the present theory of probable involvement of the hilum lymph nodes in an acute inflammatory hyperplasia, and the action on these glands in reducing their size.

The ordinary dosage for a child aged from 5 to 10 years was five minutes exposure with a Coolidge tube set at 4.0 ma., a 1 mm. aluminum filter and a 6 to 7 inch back up spark at a distance of 28 inches.

Treatments were given every alternate day for three treatments, followed by a second course beginning seven days later. Relief usually followed a few hours after the third treatment. Very few patients had more than four treatments.

HENN, Chicago.

EPIDEMIOLOGY OF DIPHTHERIA. HANSSEN, Jahrb. f. Kinderh. **104**:201, 1924.

Diphtheria appeared in Schleswig-Holstein in the first part of the nineteenth century, though it did not become an epidemic until 1860. It appeared first in the southern part and spread northward. It was distinctly a children's disease, and has remained so, the most susceptible age being from 1 to 5 years. This rather extensive study bears out the usual ideas, namely, that diphtheria is a disease of populated centers and is spread by contacts in school, church and other crowded buildings. The serum treatment has greatly reduced the number of cases and the mortality since 1894.

STUDIES ON THRUSH. BERTHOLD EPSTEIN, Jahrb. f. Kinderh. **104**:129, 1924.

This is an extensive study of thrush, particularly to determine the latent form of the thrush fungus, and its relation to the acute disease. In addition to microscopic and cultural characteristics he was able to immunize rabbits and use a complement fixation test to aid in differentiation of types. The serum of children with thrush did not, however, give the complement fixation reactions.

Of 2,000 infants, active thrush was found in 270 cases, but none during the first 5 days of life. The most occurred during the second week, and few in the second half year. Eighty-one per cent. of the cases were distinctly ill. Latent thrush was much more frequent during infancy than the active disease, and was found as early as the second day of life.

A larger percentage of pregnant women and women with children under 1 year of age have thrush, than have those not pregnant or with only older children. In all cases of thrush in the infant, fungi of the same variety were previously present in the mouth of the mother. If the mother's mouth was free of fungi, the child remained free. If the child's mouth was infected, the fungus appeared next on the breast of the mother and later in the child's stool.

Latent organisms in the mouth may cause active disease if the infant is very young, premature, weak or very icteric, or the thrush may remain latent for months and become active with the onset of an acute disease not related to thrush. Attempts to change a latent to an active thrush in new-born kittens by local application of hydrochloric acid solution and trichloracetic acid were not very successful, though they did succeed in one case. The prophylactic treatment suggested is that the mother should use a mouth wash before and soon after delivery.

SUTHERLAND, Chicago.

PYREXIAS OF OBSCURE ORIGIN IN CHILDREN. PHILIP F. BARBOUR, South. M. J. **17**:256, 1924.

Intestinal toxemias are common causes of pyrexias. In the earlier stages, these conditions are not easily differentiated from typhoid and paratyphoid. Pneumonia can be masked by pronounced intestinal symptoms. Pyelitis is frequently overlooked. It is one of the commonest causes of pyrexias. Repeated urine examinations are absolutely essential to the diagnosis. Focal infections play a large part in the production of obscure pyrexias. The tonsils are apparently the chief seat, but sinus trouble must not be overlooked and is more often responsible for pyrexias than is commonly supposed. Tuberculosis must always be thought of and its presence or absence definitely established.

SCHLUTZ, Minneapolis.

CONVALESCENT WHOLE BLOOD, PLASMA AND SERUM IN PROPHYLAXIS OF MEASLES. ABRAHAM ZINGHER, J. A. M. A. **82**:1180 (April 12) 1924.

Of one hundred and two children receiving convalescent whole blood, plasma or serum, ten developed measles. Of these, seven were injected on the eighth day of exposure and developed a modified form of measles after twenty-two days. One child injected on the seventh day of exposure developed typical measles twenty days later, after a period of incubation of twenty-seven days. The tenth child was protected by 5.0 c.c. of convalescent serum for twenty-eight days, when she was exposed to a second case of measles and developed a typical attack fourteen days later, forty-two days after receiving the serum.

Of the five control children, four developed typical measles after periods of incubation varying between twelve and fifteen days.

Of fifty-eight additional children, injected in two institutions, twenty-three developed a mild and modified form of measles and three a typical form of the disease with characteristic catarrhal symptoms. In these three children, a thirty-five day convalescent plasma was used in doses of 3.0 c.c. Of thirty-three control children, three showed a mild form and ten a typical form of measles after the usual period of incubation.

Convalescent measles serum, plasma, or whole blood can be used to produce passive immunity if injected within the first four or five days after exposure, and to modify the character of the disease when injected after the fifth day.

The dose of serum during the first four days after exposure is 2.5 c.c., during the fifth and sixth days 5.0 c.c., and during the seventh and eighth days 7.5 c.c. Doses of from 2.5 to 3.0 c.c. from the fifth to the tenth day after exposure modify the attack. These doses are calculated for children 3 years of age.

HENN, Chicago.

RHEUMATIC HEART DISEASE IN CHILDREN UNDER TWO YEARS OF AGE. B. S. DENZER, J. A. M. A. **82**:1243 (April 19) 1924.

Denzer reports three cases of rheumatic fever with heart disease, in children under 2 years of age. It was found at necropsy that these children had either subcutaneous fibroid nodules or Aschoff bodies. The author raises the question whether the present view of rarity of rheumatic heart disease in infancy might not be revised.

THE PATHOGENESIS OF RHEUMATIC FEVER. HOMER F. SWIFT, J. Exper. Med. **39**:497, 1924.

The manifold clinical signs of rheumatic fever, and the occurrence of joint pain in so many diseases, have caused much confusion in our conception of the essential nature of the disease.

Nonhemolytic streptococci have been claimed to be the causative microorganism, but the failure to recover them from the majority of patients and to reproduce the classical disease by inoculation into animals leaves the question unsettled. For a better understanding of rheumatic fever we are forced to a continued bedside study and tissue examination.

Excrescences made up of elements of the circulating blood occur along the free margins of the heart valves, at places where the endothelium has disappeared. Evidences of proliferation are seen under the endocardium in the heart valve. Characteristic lesions occur in the mural subendocardial region without primary injury to the endothelium and in the base of the valve leaflets. It is not difficult to conceive of the primary injury of the valves occurring in their substance rather than on their surface. The possibility of swollen covering endothelium being broken by impacts against an opposing leaflet is easily seen.

Lesions similar to Aschoff bodies found in the diseased pericardium indicate that the essential or primary pathologic process is similar to that found elsewhere.

The most generally recognized specific histologic lesion of rheumatic fever is the Aschoff body which is a submiliary nodule located in the myocardium. Changes in the blood vessels are common. Interference with circulation must lead to disturbed nutrition of the muscle and impulse conducting fibers. Bedside and electrocardiographic investigation indicated that the myocardium or conduction system was disturbed in about 95 per cent. of cases.

The essential histologic picture of subcutaneous nodules is similar to that of the Aschoff body.

Fahr found changes in the capsule of the knee comparable to myocardial lesions. Coombs found similar changes in a shoulder joint. The capsule of the knee and ankle revealed lesions comparable with those of the heart and subcutaneous nodules. Numerous nerves in the joint capsule and surrounding ligaments easily explain the pain. The finding of lesions in the joint capsule of a patient from whom all clinical signs of arthritis had disappeared under neocinchophen, indicates that the essential rheumatic process may go on despite these antiphlogistic drugs.

Studies of the brain in chorea in the literature indicate that the chief lesion is vascular in origin. Thrombi, endothelial proliferation, and perivascular collections of round cells with small focal changes in the contiguous nervous tissue have been described. The usual peculiar response of the central nervous system to injury would naturally cause a different histologic picture here than elsewhere.

The finding of Aschoff bodies and subcutaneous nodules in chorea support the viewpoint that the lesions in the various organs are due to a common causative agent—the infective agent, or virus of rheumatic fever.

With this conception of the essential pathology of rheumatic fever, namely, disseminated focal submiliary nodules, with edema in the contiguous tissues during the acute stages, combined with lesions of the blood vessels, it is not difficult to reconcile the manifold and apparently unrelated manifestations of the disease.

McClure, Evanston, Ill.

Chronic Infections

The Recent Recrudescence of Epidemic Infantile Paralysis. Herman B. Sheffield, M. J. & Rec. **119**:72 (April 2) 1924.

The author calls attention to the fact that there has occurred in New York another epidemic of poliomyelitis of moderate severity. He does not give the number of cases reported to the health department, but states that "as usual, a far greater number remained unreported for fear of quarantine." The author has seen eighteen cases with no fatalities, which is characteristic of this epidemic. The initial symptoms were not characteristic, as a great majority of the patients complained of severe pain in the muscles, while the paralysis did not appear until rather late (in two patients after ten days). Symptoms were attributed by many physicians to digestive disturbances, rheumatism or influenza. The somewhat detailed description of the pathologic anatomy should be seen in the original article. The author is opposed to the use of serum and apparently did not apply it in any of his cases.

Byfield, Chicago.

The Importance of the Newer Serological Methods in Congenital Syphilis. Friedrich Szirmai, Jahrb. f. Kinderh. **104**:257, 1924.

The Wassermann reaction was found to be more sensitive than the Meinicke-Trübungs, Dold, and the Sachs-Georgi reactions, which showed degrees of sensitiveness in the order named. These precipitation reactions were therefore more definitely diagnostic of syphilis than the Wassermann. Practically all of the untreated cases which were clinically congenital syphilis showed a positive Wassermann reaction, and only a few of the treated cases were negative. A few non-specific positive reactions were obtained in scarlet fever, tuberculosis, chorea minor, and varicella, more often with the Wassermann reaction than with the precipitation reactions. The Meinicke-Trübungs reaction was positive in the mothers of syphilitic children more often than was the Wassermann reaction. The using of duplicate tests, therefore, showed some latent cases, and decreased the number of uncertain reactions.

Sutherland, Chicago.

"Lues Nervosa" and the Influence of Idio and Parakinetic Syphilis on Progeny. I. Husler, Ztschr. f. Kinderh. **37**:200, 1924.

One hundred and thirty-two living children from fifty-two families, in which the mother or father or both had syphilis of the central nervous system, were studied. For comparison, the data from a series of 142 children whose parents (sixty) had visceral syphilis and from a series of 160 children of fifty-one nonsyphilitic parents were used. The results of pregnancies are given in the tables:

52 families with central nervous system syphilis—245 births.

Deaths	Per Cent.
Abortions	20.4
Premature births	3.7
Infants	17.9
Older children	4.1
Total	46.1
Living	53.9

60 families with visceral syphilis—276 births.

Deaths	Per Cent.
Abortions	26.4
Premature births	1.1
Infants	20.3
Older children	3.62
Total	51.5
Living	48.5

Over half of the children of the parents with syphilis of the central nervous system were not syphilitic, while only one-fourth of the offspring of the visceral syphilis group were absolutely free from syphilitic manifestations. Thirty-one per cent. of the children of the former group showed disturbances of the central nervous system, 30 per cent. of the latter. In the control group, no syphilis, 18.75 per cent. of the children had disturbances of the central nervous system.

Peterman, Rochester, Minn.

Experimental Observation on the "Cure" of Syphilis in the Rabbit with Arsphenamin. Alan M. Chesney and Jerold E. Kemp, J. Exper. Med. **3**: 553, 1924.

From the literature it would appear that there is no unanimity as to the possibility of curing syphilis in rabbits with arsphenamin. From experiments in which the reinoculation method was used as a test it would seem impossible to eradicate the infection once it is established. With the method of lymph node transfer as a test, it seemed possible to produce a cure in rabbits. There is no unanimity as to whether or not a successful reinoculation of a rabbit with syphilitic virus indicates the cure of a preexisting infection.

The authors attempt to answer the questions as to whether syphilitic rabbits can be rendered free of the infection by administration of arsphenamin, as judged by lymph node transfer, and whether rabbits thus freed from infection are susceptible to reinoculation with the same strain of spirochetes. Twenty-two male rabbits were infected with *Spirocheta pallidum*. Ten received six weekly intravenous injections of 10 mg. per kilogram of arsphenamin, treatments being begun 127 days after inoculation. Twelve rabbits were left untreated. From thirty-two to thirty-eight days following the final injection of arsphenamin, both popliteal nodes were ground up and injected into the right testicle of each of two rabbits. The animals were observed for ninety days before being discarded as negative.

The lymph node transfers from the ten treated animals failed to produce syphilis in all cases. The nodes from the twelve untreated animals, produced positive results in ten cases.

Reinoculation was done in both treated and untreated animals forty days after completion of treatment, or 209 days after the original inoculation. Testicular emulsion containing motile spirochetes of the same strain was injected intradermally at the base of the right ear. Nine days later a drop of the testicular emulsion was rubbed into the scarified epidermis of the left ear. Reinoculation of ten treated and nine untreated rabbits failed to produce lesions at the site of inoculation.

These experiments show that the administration of arsphenamin as described is sufficient to eliminate an existing syphilitic infection in rabbts as determined by lymph node transfer, performed from thirty-two to thirty-eight days after discontinuing treatment, when the infection has been present 127 days before the treatment was begun. These results are in agreement with those of Nichols and Walker. Whether or not these animals continued to harbor spirochetes elsewhere in the body is still debatable. Concerning the reinoculation experiment the question arises as to whether the absence of local lesions at the site of inoculation is evidence that infection has not taken place. The authors are inclined to the view that the animals were in reality not reinfected. The failure of reinoculation in the treated animals could equally well be interpreted as evidence that the animals were immune, as that they were still infected. They consider the demonstration of the presence or absence of lymph node infection a better criterion for the evaluation of an antisyphilitic agent than the method of reinoculation as carried out in their experiments.

McClure, Evanston, Ill.

Internal Diseases

Twins with Hypertrophic Pyloric Stenosis. Leslie H. Moore, South. M. J. **17**:187, 1924.

This case report is quite unique, in that the condition developed simultaneously in both twins and ran quite a parallel course. Vomiting began in the second week. The Rammstedt operation was performed successfully on both patients at the end of the fourth week. Vomiting ceased, but death ensued in one infant forty-eight hours after operation, apparently from respiratory failure, and in the second child eight days after the operation, apparently from the same cause.

Schlutz, Minneapolis.

CASE OF HENOCH'S PURPURA. DONALD KILGOUR, Canad. M. A. J. **14**:302 (April) 1924.

The author gives an excellent review of the present day knowledge of the subject. The classification of Minot and Lee is given as the most acceptable. Henoch's purpura is considered to be an idiopathic purpura other than hemorrhagic purpura, the latter term being limited to those cases of purpura showing a diminution in blood platelets.

Nothing new is brought out in pathology or treatment. The use of blood transfusion in the severe anemia accompanying the condition is stressed.

One case is reported in a boy, aged 5 years, who developed a very severe secondary anemia, with hemoglobin, 20 per cent., and a red count of 1,000,000. Transfusion with 300 c.c. of blood from his father, using direct paraffin method, resulted in a rapid cure. The unusual features in the case were severe epistaxis and the very severe secondary anemia.

MOORE, Omaha.

SUDDEN DEATH ASSOCIATED WITH THE INJECTION OF FOREIGN SUBSTANCES. R. W. LAMSON, J. A. M. A. **82**:1091 (April 5) 1924.

Lamson has tabulated the reported deaths following injection of foreign material since 1894. In one group are forty-one cases in which death may have been due directly or indirectly to the protein injected. In the other group of twenty-one cases death seemed due to primary disease or some other cause not associated with the injected substance. Diphtheria antitoxin was the protein injected in all but ten of the cases. This does not indicate an inherent toxic action of the diphtheria antitoxin itself but rather that this serum is used more frequently than any other serum. Fourteen cases gave a history of asthma or hay-fever. Previous injections had been given in eight cases and in thirty-one there was no history of injection. The treatment of asthma with diphtheria antitoxin or normal horse serum resulted in five deaths. The sex of the patient was not indicated in four cases, but in others twenty-six were males and eleven females. Most of the patients were under the age of puberty. In a majority of cases death follows in a short time. When the fatal reaction is delayed for a matter of hours, it is difficult to ascribe to the serum specific or nonspecific effect.

The diagnosis of status lymphaticus was made at necropsy in three cases. The relation of the thymus to the cause of death here, as in cases during anesthesia, is not settled. Unfortunately, in only a few cases was necropsy obtained, and in these there was no consistent pathologic finding.

A negative scratch test for hypersensitiveness is not a sufficient reason for a nonspecific reaction. In a few of the observed cases the amounts injected were so minute that it is difficult to believe that the nature of the injected substance could have very much to do with the fatal result. One is inclined to assume individual physiologic peculiarities on the part of the patient as the determining factor.

HENN, Chicago.

OLEIC ACID HEMOLYSIS IN INFANTILE ANEMIAS. KARL BENJAMIN, Jahrb. f. Kinderh. **104**:277, 1924.

Febrile infections and overfeeding with milk lead to anemia, but the mechanism of this is not well understood. Hemosiderosis in the liver and spleen, and increased excretion of urobilinogen in the stools point toward increased blood destruction rather than a deficiency in the food. The whole blood of anemic infants showed hemolysis with a lower concentration of sodium oleate solution than did the blood of normal infants. Cholesterin, which is a protective substance against hemolysis, is decreased in the anemias even more than is the dried residue. Other substances, probably proteins of the serum, also neutralize the oleate. The author concludes that overfeeding with milk, and to a greater extent febrile infections, cause anemia by decreasing the cholesterin and the albumin of the serum, thus leading to increased hemolysis.

SUTHERLAND, Chicago.

CLINICAL EXPERIENCES IN ORGANOTHERAPY WITH SPECIAL REFERENCE TO THE STIMULATION OF BODY GROWTH. T. A. McGRAW, Endocrinology, Bull. of the Association for the Study of Internal Secretions **196**:234, 1924.

The author presents a number of his clinical experiences with organotherapy, the patient in every case being a child suffering from retarded physical development. The patients are divided into two classes: (1) with definite symptoms of endocrine disease; and (2) without definite symptoms of endocrine disease. Thirteen cases are presented with their essential histories and graphic growth charts and photographic illustrations. There is a brief discussion of the cases, especially as regards rational of treatment instituted. The author gives several pertinent therapeutic suggestions. He deplores the all too prevalent practice of organotherapy in a hit-and-miss manner and stresses the importance of a careful diagnosis from the endocrine standpoint, supplemented by roentgen-ray and laboratory examinations. He condemns the prevalent use of pluriglandular mixtures, as sold by the mail order houses. He would institute treatment with the extract of the gland standing out as primarily affected, adding to this the extract of the other glands as indicated.

WADDELL, University, Va.

ABDOMINAL PAINS IN CHILDREN BEYOND THE AGE OF INFANCY. HARRY S. SNYDERMAN, M. J. & Rec. **119**:78 (April 2) 1924.

The author properly calls attention to the obscure etiology of colicky abdominal pain in childhood, excluding referred pains which are due to acute conditions. He assumes that the commonest cause is some form of indigestion, especially in those cases where a large amount of mucus is present in the bowel movement (Mucus Disease, Eustace Smith). Other causes which he includes are: irritation from undigested vegetable matter due to imperfect mastication. This latter sometimes is the result of defective teeth. Illustrative cases are quoted. Thread-worms and other intestinal parasites, constipation, cyclic albuminuria, renal calculus, movable kidney, tabes mesenterica or caseation of the mesenteric glands and biliary colic (gallstones). The case illustrating this latter condition in a child, aged 9 years, was confirmed by operation.

BYFIELD, Chicago.

Diseases of the Skin

A SURVEY OF ULCUS TROPICUM. CORPUS TEOFILO, J. A. M. A. **82**:1193 (April 12) 1924.

Tropical ulcers usually appear in cachectic persons or in barefooted school children during the wet months. They are thought to be caused by a spirochete described as Eggerts' Type A. The spirochetes may be seen in diluted carbolfuchsin stains of oozings from edges of the ulcers. The disease is contagious and is often spread by school children in constant contact with one another. Treatment is varied but the most effective is arsphenamin (3 per cent. solution applied locally), and the next is Vincent's Powder, composed of one part sodium hypochlorite and nine parts boric acid.

HENN, Chicago.

ISOLATED FAVUS OF THE EYELID. REPORT OF A CASE. SIGMUND S. GREENBAUM, Am. J. Ophth. **7**:6, 1924.

A boy, white, aged 10 years, developed a yellow, cupshaped crust on the lower lid just beneath the lashes. On removal, the underlying tissue was erythematous with epidermic infiltration and several small scattered erosions. The crust was made up of mycelium and spores. On culture the organism grown was *Achorian quinckeanum* (mouse favus).

WESCOTT, Chicago.

THE THERAPY OF CONSTITUTIONAL ECZEMA IN INFANTS. A. S. SOKOLOW, Jahrb. f. Kinderh. **104**:91, 1924.

A series of eleven infants with chronic eczema was injected parenterally with foreign protein in the form of milk, in doses of from 0.2 to 0.4 gm., at intervals of from two or four days. There was complete recovery in five cases and marked improvement in three cases, giving a good result in 73 per cent. The improvement in the eczema was definite after three or four injections. The chief reaction was a fever, at its maximum in seven hours. Only permanganate baths were used locally.

The writer suggests that even better results should be obtained if skin sensitization tests were made, and the injected protein varied, 'depending on the infant's sensitization.

SUTHERLAND, Chicago.

Nervous Diseases

SENSE PERCEPTION OF THE PREMATURELY BORN. ALBRECHT PIPER, Jahrb. f. Kinderh. **104**:195, 1924.

The effect of sound, light, pain and cold stimuli on the respiration of the sleeping infant was recorded on a kymograph tracing by means of a Marey tambour. The premature infants reacted as readily as the well developed newborn infants. The writer suggests this method to test sensation in idiots.

SUTHERLAND, Chicago.

A NOTE ON THE COMPARATIVE HISTOPATHOLOGY OF ACUTE ANTERIOR POLIOMYELITIS AND EPIDEMIC ENCEPHALITIS. GEORGE B. HASSIN, Arch. Neurol. & Psychiat. **11**:28 (Jan.) 1924.

Hassin, in his studies of a case of epidemic encephalitis and one of anterior poliomyelitis, concludes that, although grossly, the two conditions appear very similar; they have a distinctive histopathology as well as distinct clinical and serologic characteristics. He states that in both conditions there may be widespread changes throughout the brain and spinal cord and that these changes in the medulla, pons and other parts of the brain cannot be differentiated from each other in all cases. Differentiation, however, is possible by a study of the changes in the spinal cord. There the inflammatory changes are usually much more marked in anterior poliomyelitis, in which the smaller capillaries are involved. However, the distinguishing point is the fact that the degenerative changes in the motor neurons are far greater in anterior poliomyelitis than in epidemic encephalitis. Also that in the former these changes are confined to the motor neurons, as is not the case in the latter. In anterior poliomyelitis the degenerative and inflammatory changes decrease in severity in the medulla, pons and cortex, while in epidemic encephalitis the changes are most marked in the brain, and decrease in severity in the spinal cord. There were also found in the central canal of each cord hemotogenous elements resembling those present in the perivascular spaces and in the parenchyma. This, the author points out, may be interpreted as a proof that the flow of the contents of the perivascular spaces is not only toward the subarachnoid space but also toward the central canal.

FAMILIAL MUSCULAR DYSTROPHY. H. P. MILLS, THOMAS H. HAINES and MINA A. SESSIONS, Arch. Neurol. & Psychiat. **11**:43 (Jan.) 1924.

Mills, Haines and Sessions report a series of six cases of muscular dystrophy occurring in one family. Five were boys and the other a girl. All but one boy, who died of pneumonia at the age of 19, are living. The ages of the remaining children range from 9 to 29 years. The boys all suffer from primary type of atrophy, affecting the shoulders and arms or trunk and thighs. The girl suffers from the pseudohypertrophic form and is the eldest of the children affected. The facial muscles were unaffected in all the patients. The condition appeared in all the children at the age of 7 years. In one of the boys, a contracture was present in the hip joint but was not found in any of the others. Examination of the blood and spinal fluid revealed no abnormalities. The blood sugar was found to be within normal limits. Basal metabolic rates were taken on the five living children and ranged from a minus 22 to a plus 10. No abnormalities were brought out by roentgen-ray examination of the skull. Vasomotor disturbances were present in practically all cases. The authors point out that the one case of the pseudohypertrophic type, occurring in the eldest girl, does not conform to the characteristics reported by Gordon, who stated that such cases usually die young, were more frequent in boys and are apt to present no history of other cases in the family. There were five other children in the family who were healthy, and no such trouble was present in the eleven grandchildren, ranging from the age of 1 to 11 years.

AVERY, Chicago.

Diseases of the Eye

ETIOLOGY OF KERATOMALACIA. EUGEN STRANSKY, Jahrb. f. Kinderh. **104**:183, 1924.

The writer presents two cases of keratomalacia which were typical avitaminosis and hypovitaminosis. The former patient improved rapidly on cod liver oil and butter, though the latter, a patient with pyloric stenosis with marasmus, died. Other cases which developed in the course of other conditions, such as dysentery (Flexner type), severe chronic dyspepsia, and acute dyspepsia could not be ascribed to a lack of vitamin A in the diet. These patients all died. The conclusion is that xerophthalmia is dependent on a lowered resistance of the whole organism and especially of the cornea to infection of any kind. This lowered resistance may be due to avitaminosis or hypovitaminosis or to enteral or parenteral infections. In the latter cases vitamin A is without effect on the xerophthalmia.

SUTHERLAND, Chicago.

HEREDITARY CATARACT. ALBERT L. BROWN, Am. J. Ophth. **7**:33, 1924.

Three generations of descendants of one family have been under observation since 1911. Of eight descendants of the first patient seven have congenital cataracts. In each case the transmission was from a female, but both sons and daughters were affected. The husbands had normal eyes and there was no blood relationship between husband and wife. Nothing new is added by the author as to whether the defects are developmental or metabolic, but he does stress the sociologic question of marriage among such persons and reports that the answers to questionnaires sent to ophthalmologists and superintendents of homes for the blind showed the majority in favor of limitation of marriage.

WESCOTT, Chicago.

Surgery and Orthopedics

Correction of Structural Lateral Curvature of the Spine. R. W. Lovett and A. H. Brewster, J. A. M. A. **82**:1115 (April 5) 1924.

The authors are using in treatment of organic or structural scoliosis, a new jacket that will comfortably correct and at the same time permit of mobilization of the spine.

Silent Foci of Localized Osteomyelitis. D. B. Phemister, J. A. M. A. **82**:1311 (April 26) 1924.

In four cases reported, Phemister found osteomyelitis lesions which had proceeded to the stage of complete destruction of the bone area involved, with surrounding new bone formation before there were any local symptoms whatsoever. The only places where symptomless osteomyelitis has been thought to develop were pockets about the roots of teeth. These are not thought to be related to the silent foci which usually arise as complications or sequelae of diffuse staphylococcus osteomyelitis. Phemister suggests that sometimes a routine search by palpation and roentgenography is indicated, and that these silent foci may explain localized symptomless areas of bone sclerosis.

Henn, Chicago.

A Case of Massive Hypertrophy of the Breasts in a Young Girl. Thew Wright, Bull. Buffalo Gen. Hosp. **2**:31, 1924.

Wright reports a typical case of puberty hypertrophy of the breasts, and calls attention to the fact that it may be due to an endocrine imbalance, whereby the normal inhibitory influence to mammary hypertrophy fails to act at the proper time.

Bacon, Chicago.

Congenital Cystic Dilatation of the Common Bile Duct. G. L. McWhorter, Arch. Surg. **8**:604 (March) 1924.

The author operated on a woman, aged 49, who had been suffering from attacks of pain in the right upper abdomen associated with jaundice since she was a baby. She had previously had a drainage of the gallbladder performed. His findings at operation were extremely interesting. The gallbladder was small and distinctly differentiated from a dilated cystic duct by a narrow constricting sphincter of scar tissue and muscle. The cystic duct opened into an enormous balloon-like common duct, that apparently had no communication with the duodenum which could be demonstrated. This cavity contained several small cholesterin stones as did the greatly dilated hepatic ducts. The dilated common and cystic ducts were removed and an anastomosis made between the duodenum and hepatic duct. The patient made an excellent recovery, in spite of a temporary duodenal fistula.

The literature contains the records of but forty-seven similar cases, none of which was diagnosed before the abdomen was opened. The condition is a progressive one, and a good prognosis is dependent on early operation and effective internal drainage of the bile. Of this series, including the author's case, only nine were successfully operated on and permanently cured.

In view of the difficulty of the preoperative diagnosis, we believe that the recent experimental work of Evarts Graham on detection of abnormalties of the gallbladder by means of a dye excreted through the bile and casting a shadow in the roentgen-ray picture would materially aid in such a case as this one.

Congenital Deficiency of the Diaphragm. E. C. Cutler and S. F. Cooper, Arch. Surg. **8**:506 (March) 1924.

There are three classes of congenital lesions of the diaphragm (1) true hernia with a sac covering the displaced intestine; (2) false hernia, or hernia without a sac; and (3) eventration. The diaphragm develops from four different sources: Its ventral pericardial portion is formed from the septum transversum, its lateral portion from the pleuroperitoneal membranes and the medial dorsal portion from the primitive mesentery. Its muscular portion comes from a pair of premuscle masses which lie on each side of the fifth cervical somite. This muscle goes caudad with the septum transversum, carrying the phrenic nerve with it, and develops chiefly in the dorsal portion of the diaphragm. According to Hume, the types of congenital diaphragmatic hernia may be classified as arising as follows:

1. Through the hiatus pleuroperitonealis. This is the commonest type and is probably due to the intestine following the lung bud as it leaves the abdominal cavity (always false).

2. Through the dome of the diaphragm. This may be true or false and may be caused by a weak point in the diaphragm. These cases are often associated with incomplete rotation of the intestine.

3. Through the esophageal orifice. The stomach may fail to migrate below the diaphragm or may migrate late, leaving a large esophageal opening.

4. The entire left half of the diaphragm may be absent, a very rare condition. The fact that congenital deficiency of the diaphragm occurs much more frequently on the left than the right may be explained by the distribution of the vascular elements which play such an important part in the early formation of the embryo. The vascular concentration in the region of the right side of the diaphragm would contribute to the strengthening and blocking of the pleuroperitoneal canal, while atrophy of the common cardinal vein on the left would contribute to the weakening of the left half of the diaphragm.

The authors in operating on an 8 weeks' old puppy, observed that the animal had great difficulty in attempting to vomit and finally died on the table. At necropsy a congenital opening was found in the anterior part of the right diaphragm and through this opening had passed the fundus of the stomach, the spleen, part of the great omentum, about two thirds of the liver and the gallbladder.

In children, the symptoms of such a lesion are usually due to herniation through a relatively large opening of a considerable part of the abdominal gastro-intestinal tract, occurring as a result of straining or changing position, giving rise to an acute dyspnea with asphyxia. Examination should reveal unusual tympanitis in the chest and obscure breath sounds. If the opening is small, a loop of bowel may be kinked and give rise to signs of obstruction. In the majority of cases, however, there are no unusual symptoms at all or merely indigestion. Roentgen-ray examination should make certain the diagnosis and differentiate between the types. Treatment must be surgical if the severity of the symptoms warrant any interference at all. The thoracic route is the one of choice. By excision of the sixth, seventh or eighth ribs posteriorly and laterally, an excellent exposure of the diaphragm is obtained.

Miller, Chicago.

Unrecognized Fractures of the Skull in Infants and Children. Alfred W. Pollak, M. J. & Rec. **119**:65 (April 2) 1924.

This is a clinical article giving six case histories of traumatic fracture of the skull in children over 3 years of age. Three roentgen-ray pictures are shown. The author classifies the future effects as follows: (1) most fractures without depressions become absolutely well; (2) cases of mild concussion with loss of consciousness for a few seconds often show subsequent changes in disposition; (3) chronic headaches, usually of a constant dull aching type; (4) inability to stand high temperatures; (5) epilepsy, due to irritation, produced by bony spicules from depressed internal table, with blood effusion, resulting in thickening of the meninges and the formation of cysts, either beneath the site of the injury or on the opposite side.

He concluded by stating that many of the obscure brain conditions of later life may have their origin in a mild degree of concussion and suggests that every case where a child has fallen or been struck upon the head, a roentgen-ray examination of the skull be made and careful history taken in order that nothing be overlooked.

Appendicitis and Peritonitis Complicating Scarlet Fever. Benjamin Newman, M. J. & Rec. **119**:80 (April 2) 1924.

The author believes that scarlet fever is rarely followed by acute appendicitis or peritonitis developing during the eruptive stage or during desquamation. After referring to ten articles in the literature, he gives the experience of a case of his own observation. The patient, aged 6 years, was suffering from typical scarlet fever. On the fifth day the temperature rose to 102 F. and abdominal pain complained of. Operation was performed and localized appendicular abscess discovered. The recovery was without complication.

Byfield, Chicago.

Miscellaneous

Postdiphtheritic Paralysis. Alan G. Terrell and David H. Hallock, M. J. & Rec. **119**:68 (April 2) 1924.

This is a clinical article, with two case reports, one of a child aged 3½ and the other 21 months, both of which died. The first patient was given 3,000 units of diphtheria antitoxin. Paralysis appeared one month after the onset of the disease at which time the child was admitted to the hospital, dying a few days afterward. In the second case, 20,000 units of antitoxin were given. Paralysis followed five weeks later. The first patient died of respiratory paralysis and the second, of paralysis of the heart. The authors urge the preliminary giving of antitoxin before the culture report has been returned. They are also impressed with the importance of passively immunizing all contacts. They might well have called attention to the importance of prophylaxis through active immunization with toxin-antitoxin.

Juvenile Tabes Dorsalis with Destruction of Hips from Charcot's Disease. Walter G. Elmer, M. J. & Rec. **119**:70 (April 2) 1924.

A case report of Charcot's disease, developing in a girl aged 14 years, who, while doing gymnastic exercises, was thought to have dislocated her right hip, is presented by this author. When surgically treated by an orthopedic surgeon, a diagnosis of syphilis was made and treatment with neoarsphenamin begun. At that time the knee reflexes were found to be absent and the pupils did not react to light. When examined four years later, the same findings, together with Romberg's sign, were also noted. Blood Wassermann was negative with the spinal fluid strongly positive. Four years afterward, both tests were negative.

London Letter. M. J. & Rec. **119**:370 (April 2) 1924.

The recent epidemic of influenza in Great Britain has led to a marked increase in the infantile death rate. Whooping cough was also partly responsible for this increase.

RELATIONSHIP OF INFANT AND CRUDE MORTALITY RATES. DWIGHT M. LEWIS, M. J. & Rec. **119**:76 (April 2) 1924.

The author's conclusions appear in his summary, which reads thus: "yearly variations of infant mortality rates in cities where so-called standard measures for its reduction have been effective for years without decreasing such variations, statistically as well as epidemiologically, would seem to be influenced by the respiratory factor of the crude mortality rate."

THE CHILD FAMILY RELATION: A PSYCHOSEXUAL STUDY. J. F. W. MEAGHER, M. J. & Rec. **119**:88 (April 16) 1924.

This should be read in the original. The following sentences are taken at random.

Compensatory traits cover feelings of inferiority or of insufficiency. Compensations are to hide tendencies of an opposite nature; this being a self defense mechanism. Most normal people feel the need of developing self respect and of acquiring social esteem.

A person may inhibit the ideas of sex but not the energy.

Sex undergoes marked depression in all children from infancy, but is greater in girls than in boys . . . Without doubt, the most important lesson to learn in child psychology is to bring up the child so that at the end of adolescence it will effectively emancipate itself from the family. . . The acts of the family have great social value. . . Nervous types very readily absorb the home difficulties. Family feuds are often very intensive and constitute a great hindrance to the nervous patient in such a family. It is well to remember that there are two extreme ways of training a child. One is that of excessive love and coddling and the other is with a lack or absence of love and too great severity. . . It is really a bad mistake on the part of the parents to try to inculcate ideas that everything relating to sex is shameful or degrading. . . Certainly it will be admitted that the absence of happiness in a nervous individual is clinically of more importance than the presence of a dermatographia or an indicanuria.

CHILD WELFARE. M. J. & Rec. **119**:367 (April 2) 1924.

The following recommendations were made:

Infant rearing centers: It was recommended that, because of the difficulty of supervising the care of infants placed out promiscuously, rearing centers be established under the direction of qualified medical officers.

Improvement of day nurseries: (1) All crêches should be under the direction of a physician; (2) separate rooms should be used for the cradles, the linen, disinfecting purposes and isolation of patients; (3) they should be open to the pupils of puericulture schools.

School hygiene: Close cooperation should exist among the teacher, the school physician and the school nurse. The teacher should be acquainted with the fundamental principles of hygiene. Each child should be submitted to an annual examination, of which a record should be kept, and proper action taken as indicated by these examinations. The attention of the public authorities was called from the point of view of prophylaxis, to the importance of the medical examination from the point of view of the teacher and to the value of dental hygiene.

BYFIELD, Chicago.

Book Review

SELECTED ESSAYS ON ORTHOPAEDIC SURGERY. By Newton M. Shaffer. New York, G. P. Putnam's Sons, 1923. $5.00.

This volume, comprising essays on orthopedic surgery by Dr. Newton M. Shaffer, is typical of the writings of his day. They were mainly published in the late seventies and eighties of the nineteenth century.

It is particularly interesting to read the essays on chronic joint diseases, dealing with hip joint, ankle and spine. Shaffer's contention that conservatism is to be preferred to radicalism, is borne out by the present day teaching. At the time of his writings there was a wave of radicalism, in the treatment of tuberculous joints, sweeping the surgical world, particularly in hip joint disease, where excision was being widely advocated. Shaffer took the stand and proved that his results were better by conservative means than by operative procedures. The old controversy in the treatment of the hip joint diseases was then waging, that is, fixation versus extension, and the author's stand here again is borne out by subsequent experience, that is, that extension particularly in the acute and subacute stages is essential.

His teaching, that tuberculous abscesses should not be incised and drained, also has stood the test of time. It must be remembered that the tubercle bacilli had not been identified at the time many of these essays were written, and the disease was called strumous, scrofulous, and so forth.

Dr. Shaffer was a pioneer in the orthopedic work in America, and it is owing to the efforts of men of his type that the specialty today stands on the firm basis that it does.

The close clinical observations that these men carried on, so well evidenced in Dr. Shaffer's essays, might well be emulated today. Too great dependence on laboratory findings tends to weaken the clinical acumen of the modern medical man.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Cook County Hospital, Nov. 20, 1923

H. W. Cheney, M.D., *President*

Congenital Syphilis. Presented by Dr. Arthur W. Stillians (by invitation).

The first patient, a child, aged 2 years, illustrated symptomless syphilis. The child was brought in with condylomas but is now free except for slight staining where the condylomas were. The shape of the head and the carious upper incisors and first molars were suggestive. The feet were underdeveloped, and the child was mentally backward.

The second patient, a colored child, aged 5 months, had an enlarged epitrochlear gland and a maculopapular eruption around the anus, as well as a few inflammatory lesions which were not syphilitic. The principal features were the stains of the papular pigmented syphilid, which occur in both the white and colored races, and leave pigment for a long time. The child's hair looked as if it were worn off, the only kind of alopecia described in congenital syphilis, and Dr. Stillians thought it was due to rubbing rather than to the disease. A prolific growth of hair has been described as a symptom of syphilis, the so-called "syphilitic mop," but Dr. Stillians said he had never seen one.

The third case was in a boy, aged 7 years, who had a scar and also a recent gumma on the forehead. His teeth were in bad condition, the two central teeth sawedged in the manner typical of congenital syphilis. The upper front teeth were all mixed up and it was difficult to differentiate as to incisors and canines, none of them were notched, however. The gum was shrunken and the roots were exposed on one side. The molars were carious on one side both above and below. There were swellings of both the radius and ulna, due to periostitis. The lesions were bilateral and symmetrical in many places. A typical saber tibia and an enlarged epitrochlear gland were present on one side. Glandular swelling is not as reliable in congenital syphilis as in the acquired type. This patient was a brother of the first patient shown.

Dr. Stillians was interested in the differential diagnosis between the lesions of congenital syphilis and ringworm. The circinate syphilids in children usually have a narrow border of considerable height, smooth, and ranging in color from that of the skin to dark brown. The lesions of ringworm usually show vesicles or scales on a wider, less sharply elevated border.

The diagnosis between pemphigus neonatorum and bullous impetigo often comes up and is of great importance. The pemphigus lesions are usually found on the palms and soles and adjacent areas on the arms and legs, while the impetigo begins wherever the infection takes place and spreads asymmetrically over the body. Those Dr. Stillians had seen in syphilis were vesicles which were fairly thick walled. In bullous impetigo the lesions are very superficial, rupture very early and are usually larger than those of syphilis.

He was especially impressed some months ago with the difficulty of making a prognosis in congenital syphilis. The textbook rule is that the prognosis is worse according to the time and amount of eruption—the earlier and more marked the eruption, the worse the prognosis. In two cases observed at the same time in the hospital one presented a bullous syphilid which extended not only over the arms and legs, but over the trunk as well. It was the most marked case he had ever seen and came on soon after birth. The eruption in the other baby came on three or four weeks after birth with a very scanty distribution of papules. They expected the first baby to die and the second one to get well but the reverse happened, and he was more guarded than ever in regard to prognosis in these cases.

COMMON FOOT DEFORMITIES IN CHILDREN. Presented by DR. BEVERIDGE H. MOORE.

In thinking over this subject it seemed to me that a very easy way to treat it was to divide the deformities into three classes: First, the deformities that are noticed before the child walks; secondly, those that are noticed after the child walks and, third the deformities of the feet, which appear in late childhood or early youth.

The most noticeable deformity in the early period before the child begins to walk is the congenital clubfoot, of which the equinovarus is the most common. It may be either bilateral or unilateral and there is no trouble in the diagnosis at birth. The only thing to look out for is to be sure that the condition is not due to spina bifida, because those cases give a different prognosis from the ordinary clubfoot.

As to treatment, the best plan is to start stretching and massage as soon as possible after birth. The mother can carry on this treatment until the foot is stretched and loosened, during the first month or six weeks, and then it is not nearly so hard to cure later on. When the child is about 6 weeks old I like to begin putting on casts, a plaster bandage being put on to correct the foot and twist it around gradually to a normal position so that it will be held and the bones will gradually grow in the position they should be. By doing this early one can often save the child an operation, or if an operation is necessary a simple tenotomy can be done later.

The valgus deformities are not so common but are occasionally seen. They are usually associated with deformity of the tibia or absence of the fibula.

Another deformity that is noticed early is the presence of supernumerary toes, for which the only treatment is removal. It seems to me it is well to wait for this until the child is gaining well, and in good condition generally, that is, some time during the first year because the child has not yet learned to walk and there is much less trouble in learning then.

The deformities noticed before the child begins to walk are nearly all gross deformities. We sometimes see flatfoot before the child walks but it is not of much significance. Most children have a low arch with a large pad of fat, and there is not much difference in the shape of the child's foot then.

Taking up the deformities that are noted after the child begins to walk, they are much more frequent, but not so marked. The first is weak ankles. The inner malleolus may almost touch the floor and the whole foot will be rolled outward. Those conditions can best be treated in little children by having the shoe built up on the inner side so that the weight is thrown to the outside of the foot, thus giving the ligaments and muscles on the inner side a chance to shrink and take up their work. It is difficult to get a child of this age to take regular exercise, and the easiest way to treat them is to have laced shoes with heavier soles than usual and have them built up so that the weight is thrown to the outer side. The mothers invariably ask about the so-called "weak ankle" shoes but I never thought they did any good.

Another thing the mothers notice is that the child toes in. This is really rather a good fault because if the child walks pigeon-toed it means that he is getting a good gripping action of the toes and this usually results in a good, sound pair of feet later on. Unless it is too marked and the child gets one foot in front of the other, it is hardly necessary to do anything for it. If necessary, one can have the shoe built up on the outer front part of the sole so that that part comes in contact with the ground first, thus twisting the foot out. Turning the foot out, or everting it is worse because it throws more strain on the ankle. It can be much more easily corrected than the other condition by having the heel built up on the inner side as well as on the sole, tending to throw the foot inward.

Taking up the deformities appearing in late childhood or early youth, we then see the flatfoot when the patients are about 11 or 12 years old. We often get a history of a child growing very rapidly for a time, and then the mother begins to notice that the feet are weak and the arches come down. This is a matter of the child outgrowing its strength, and the muscles of the feet not keeping pace with the rest of the body. It is a good plan to use foot plates or metal arches, because you want to strengthen the arches and make them do the work. I believe the best treatment is to have a child wear a fairly wide shoe, well fitted, with a good shank. The principal thing is to get the muscles of the leg and arch built up so that they will support the foot and then it will be permanently well. That can be done by developing the muscles on the bottom of the foot and the tibialis anticus and tibialis posticus.

The cases should be classified, and exercise must be carefully graded and planned with considerable skill to have them done right. It is also a good plan to build up the shoe so that the foot will turn inward, throwing the weight slightly on the outer side.

Another deformity seen quite frequently about this time is hollow foot, feet that are contracted so that the weight bearing comes on the ball of the foot and on the heel. In these cases the toes are often retracted to a greater or less extent. Those cases come in different groups and need considerable support from a good, well fitted shoe that fits up under the arch. A good, wide heel of considerable height is necessary that will raise the heel well off the floor. Sandals for feet like this lead to a great deal of trouble. This hollow foot is one of the worst deformities that is seen although people very frequently are proud of the high arch.

Another thing that causes deformity of the feet is infantile paralysis. In all such cases deformity of the feet is due to unbalanced action, the stronger muscle outpulling the weaker. The main thing to do is to build up the weak muscle by exercise but this must be carefully graded. It does not do to tell the parents to have the child exercise and the foot will come out all right, for walking in these cases is very often very harmful and the child should have carefully supervised exercise as well as properly fitting braces to prevent the development of deformity.

A CASE OF CLEFT PALATE AND HARELIP SUCCESSFULLY REPAIRED. Presented by DR. HERBERT A. POTTS.

Dr. Potts believes that first and last these cleft palate babies belong to the pediatrician. In many instances it would be criminal to try to repair a cleft palate in these tiny little things. (Pictures were here shown of emaciated infant.) This child came in three weeks ago in a worse condition than at present and has been under the care of a pediatrician since then. It is now in fair condition and will be checked up until the child is on a straight road to health. The nutrition is poor, the circulation is poor and any operation is likely to be a failure. Such cases belong to the pediatrician before and after operation.

As death at times occurs on the operating table, and some patients develop a high fever after operation, we should always be suspicious of a "lymphatic state." We can demonstrate a considerably enlarged thymus by means of the skiagraph and this precaution should be taken in all infants. If an enlarged thymus is found, operation should be deferred for some weeks or months during which time the enlarged gland can be reduced by means of roentgen-ray therapy.

In cleft palate and harelip I believe that the anatomy of the soft parts is practically complete in most cases and that the cleft is simply the result of the nonunion. The bony vault of the cleft palate is high, and the sum of the soft tissue is usually sufficient when dropped down to bring it together in the midline. The different types result from failure of union of the different portions. I saw recently a simple harelip with a split uvula, the palate and alveolar arch were complete. We frequently see just the split uvula. Then there is the double cleft palate in which the vomer is hanging loose in the vault, and the single one in which the right side may be perfect while on the left side the floor of the nose is absent. We may have a simple notch in the alveolar border or a simple notch in the lip. The majority of these deformities occur on the left side. In the double complete we have the double cleft of the lip in which the premaxilla is swung away out on the nose.

The cleft palate babies are not infrequently deficient in many ways. A certain number are idiots, and it seems the number of mental derangements is greater than in the otherwise normal babies. This picture (showing photograph) is that of an imbecile with a double cleft palate and harelip. The parents were anxious to have the appearance improved, so we repaired the lip but did nothing with the palate. There are not infrequently deformities of other parts of the body, a spina bifida, polydactylism, horseshoe kidney, absence of some of the toes or fingers or absence of the forearm or leg not due to pressure amputation by the cord.

This picture (indicating) shows a single cleft palate of the left side with an almost total absence of the forearm. This child has a lip cleft in the midline, a truncate nose, absence of vomer, meningocele in the vault of the pharynx, cleft palate, divergent squint and undoubtedly is a Mongolian idiot. (Showed series of pictures of different types of deformities.)

Of course, primarily, it is the care of these patients and not especially the repair of the deformities which should interest us. That means the children should be in good physical condition and gaining in weight. I think they are all pediatric problems. There is one common type of cleft palate and harelip in which there is a split in the arch combined with the harelip, which deserves special mention. These babies should have adhesive plaster strips placed across from in front of the ear on the well side; that is, on the long arm of the arch to in front of the other ear. The arch is usually swung out and there is protuberance of the lip on the long side. If the cleft in the lip is brought together, the plaster being cut out to accommodate the lip and nose, and the plaster is put on taut and kept tight daily, there will be a very much smaller cleft in the palate when one wishes to operate, and furthermore, the protuberant long arch will be pressed back into place. Excoriation of the skin can be avoided by cutting out the central portion and by restrapping it, putting the new plaster on top of the old.

As to the time to operate, in both cleft palate and harelip the ideal time is right away, in the first place on account of less scarring of the lip, and second because if the deformity is allowed to go on the high arch gradually flattens out. There is less space between the soft palate and the posterior wall of the pharynx in the infant than in the child 2 years old. Consequently, if perfect speech is to be attained it is necessary for the soft palate to close off the nasopharynx. If we wait until the child has grown, that space is greater and it is more difficult to restore the function of the palate. So it seems the best time to operate is the earliest, within a day or two or three for the lip, alveolar arch and nose, which we prefer to repair first, and then repair the hard and soft palate. At times we see that the mucoperiosteum is very thin and anemic. In these cases we prefer to make preliminary delayed flap operation, dissect it up from the bone and do nothing else for two or three weeks. By that time the flap is vascularized and the chances for good repair are better.

The repair of the nose is the most difficult. We have to make a floor for the nose and consequently we use all the mucoperiosteum we can. The majority of cleft palates repaired by the sliding mucoperiosteal flap result in a new bony palate. There are enough osteoblasts sticking to the periosteum to form a new bridge underneath. There are three general types of repair. Dr. Brophy brings the maxillary bones together before the third or fourth month when the bones are pliable, and holds them there by means of wires passed through the bones and twisted over lead plates. Another type proposed by Lane is one in which the mucoperiosteum is dissected up and reflected across the cleft leaving a raw surface exposed. The operation of choice is that of von Langenbeck. The soft palate must be cut away from the posterior border of the hard palate in many instances in order to close the cleft. The one thing to be especially feared is shortening of the palate by scar contraction, as any raw tissue in the mouth will heal over by scar formation. On the nasal surface there is a denuded space which results in the shortening of the palate and this we always wish to avoid. We try in a number of different ways but whether we will succeed or not is problematical. As it is, we are careful to put some sutures on the nasal side of the soft palate in order to bring the mucous membrane in apposition, and leave as little denuded surface as possible.

The after care of the lip is very important and these edges must be kept absolutely sterile. Little scars that we pay no attention to on other parts of the body look bad on the face and we should always try to avoid them. Horsehair is the most suitable suture material. It produces no pressure necrosis and if the little serum that oozes out is kept away there is no scar. The food should be sterile, and if it does not cause too much disturbance the parts should be irrigated by the douche can or syringe.

At times the babies do not eat and it is desirable to feed them by gavage. Passage of the nasal tube is not difficult but passage of the tube by mouth may result disastrously.

Speech defect is important and much depends on the parents in teaching the child to speak slowly and distinctly, especially the consonants. One of the best ways to accomplish this is to teach the child or adult a foreign language. It is very difficult to correct the speech defect by repairing the palate of the adult, as the nasopharyngeal space has increased with the growth and as a rule better speech can be attained by means of an obturator. (A stereoscopic picture of a cleft palate and harelip was shown, with lack of union of the columella nasi and lip.)

Clinical Cases. Presented by Dr. H. E. Irish.

Case 1.—A colored boy, presented because he showed a combination of things that are rather unusual. He had a neoplasm on the chest wall which contained pus, and which had been in existence for some time as a chronic abscess. It was attached to the sternum, which seemed to be thickened at the edge and then cupped out. The abscess had existed for about two months. There was pathologic change within the thoracic cavity as well as without, there being flatness in the region upward and outward from this area. No breath or voice sounds were transmitted. The area of flatness extended practically over the upper portion of the chest, the lower portion being approximately normal. Dr. Irish thought there was probably a circumscribed mass in the chest cavity as well as without. The roentgenograms verified the clinical findings.

The Wassermann and Pirquet reactions were negative. Aspiration of the chest wall gave a serous, very flaky and thick fluid. This was negative for bacteria and had been inoculated into animals. The insidious onset of the trouble and absence of cough or pain had made the condition a little puzzling. There was no history of a previous acute infection. The blood count showed 6,000 white blood cells, 55 per cent. small mononuclears, and 42 per cent. polymorphonuclears.

The question was whether the case was one of tuberculosis, syphilis, actinomycosis or a circumscribed empyema pointing at the location of the abscess. They were not yet sure as to the diagnosis, but thought that it was probably a case of tuberculosis, without positive confirmation in all directions. The patient was not sick, he was taking plenty of nourishment and his appetite was good.

Case 2.—Laryngeal stenosis. A white child, the interesting features of whose case were the many reasons for the dyspnea. The patient had been in the hospital several times because of acute dyspnea and had shown many other conditions, among them a chest picture which corresponded with the shadows that are associated with enlarged thymus. He had also had a positive Klebs-Loeffler bacillus smear from the throat. His case had at one time been diagnosed as active diphtheria, and at other times he was considered a diphtheria carrier. In addition to that, during his long stay in the hospital he was suspected of having syphilis, because of condylomas. The dark field showed spirochetes and the Wassermann reaction was four plus. The Klebs-Loeffler bacillus organisms had been cleared up and the patient had improved greatly on active mercurial treatment, but apparently the thymus persisted. Direct laryngoscopic examination showed a thickening of the laryngeal wall posteriorly, but there was no other demonstrable lesion at that time. It was a question as to whether there was a syphilitic laryngitis plus an enlarged thymus, as well as at one time a laryngeal diphtheria. At the time of presentation the child was very hoarse and more out of breath than usual, due to an acute upper respiratory infection.

Ventriculography. Presented by Dr. George Davenport.

Ventriculography was first introduced by W. E. Dandy in 1918, and to him is due not only the credit but to a large extent the clinical application thereof. More recently he has changed the terminology from ventriculography to cerebral pneumography. This term is more suitable and broader in its meaning, because often we not only see the outline of the ventricles on the plate, but the various passageways for the cerebrospinal fluid. Up to the present time we have done forty-five of these procedures.

Ventriculography, or cerebral pneumography, as we have practiced it is the replacement of the cerebrospinal fluid with air, in order to make the outlines of the ventricles and the passageways of this fluid distinctly visible on the roentgen plate.

The introduction of air can be accomplished by the intraventricular method, and when the fontanels are ossified we resort to a trephine opening in the skull, while in the infant we go through the open fontanel. The other method is by way of the intraspinal introduction of air. We have utilized both methods as indicated, always avoiding the intraspinal method whenever we felt there existed a tumor in the posterior fossa. In the intraventricular injection of air we always enter at a point anteriorly, which corresponds to Kocher's point of election. Entering at this point, the needle goes through the frontal lobe and enters the ventricle at the junction of the body with the anterior horn. After the obturator is withdrawn from the needle we attach a syringe with a two-way petcock. The fluid is withdrawn gradually, 5, 10 or 15 c.c. at a time, replacing the same by atmospheric air before more fluid is removed. This is repeated until we have removed as much fluid as possible. The patient lies with the neck flexed, face down and looking to the left.

The same procedure is followed in the intraspinal injection of air, except that the patient lies on the side with the head of the table tilted up at an angle of about 15 degrees. As soon as the injection is completed the pictures are taken, this is especially important when only a small quantity of air is introduced, so as to obtain pneumograms before absorption or dispersion of the air takes place.

We take four views as a rule, two lateral, one anteroposterior and one posteroanterior view. In the lateral views the saggital plane is kept parallel to the plate, while in the other views the saggital plane is kept at right angles to it. In all the work we have always maintained a definite distance from the plate to the target. In doing this we believe we can arrive at as nearly an accurate idea of the size of the ventricles as is possible in a human being, taking into consideration the numerous variations.

The time of exposure is the same as for any head picture, bearing in mind the fact that the infant's skull is more easily penetrated.

We have experienced what we have termed a compulsory gradual emptying of the ventricles brought about by a distortion or narrowing of the foramen of Monro on one side, so the fluid flows very slowly from the opposite side to the ventricle entered by the needle. This narrowing of the foramen of Monro is brought about by edema or a displacement as the result of a tumor.

The danger of emptying too rapidly is that it produces headache, nausea and vomiting, which is avoided by the gradual emptying.

All of our work has been done under local anesthesia in infants and children up to 9 years of age, as well as in adults. (Showed series of slides demonstrating different cerebral lesions.)

Towne of California introduced the taking of four additional views, using the horizontal ray which indicates the fluid levels as well as the proper change in the location of air which results when the position of the head is changed. These additional views add to the composite and aid in arriving at a definite roentgen-ray interpretation.

The communicating types of hydrocephalus are difficult to treat; here the intra-abdominal drainage has been attempted but reported more or less of a failure.

Indications for cerebral pneumography are: 1. In cases where a tumor cannot be localized by other means. 2. In cases operated on and no tumor found. 3. In cases which exhibit secondary manifestations so pronounced as to completely overshadow the early clinical symptoms which result from general pressure phenomena, displacement or edema. 4. As a corroborative procedure when it is necessary owing to the fact that the clinical history, the examination of the patient and observation has not been sufficiently conclusive to aid in the localization of the tumor. 5. To gain information as to the size and extent of the tumor. 6. In cases of hydrocephalus in determining the site or location of the structure which causes this accumulation of fluid. 7. In localization of the origin of a tumor, as in the case of brain tumor existing for some time suddenly developing Jacksonian epilepsy, which may result from either extension, pressure, hemorrhage or edema and yet the tumor may originate in the extreme frontal region, subcortical or parietal areas. This permits of the opening of the skull directly over the tumor rather than a wide opening over the motor region, often far removed from the tumor. He believes ventriculography is another method added to our already well known methods of diagnosis of intracranial lesions and urges its use as a laboratory method of procedure and not as a direct method of diagnosis.

Question: What is the direction of the needle?

Dr. Davenport: We enter at Kocher's point on the right side, the point of the needle directed slightly backward and inward, going in about from 4 to 5 cm. in the average case. In three instances we have struck the tumor with the needle, when we promptly entered on the other side in order to verify these facts.

Question: Have you seen any untoward results appear suddenly?

Dr. Davenport: No case has been lost from the ventriculography procedure. Some patients have had nausea and vomiting but this usually passed off promptly, providing one replaced the fluid by air and did not resort to inflation of the ventricles.

A REPORT ON TYPHOID IN CHILDREN. Presented by DR. MAURICE BLATT.

We have six cases of typhoid in the Children's Hospital today. The last patient was admitted about two weeks ago. This is a decided increase over the number of cases of typhoid in the city last year. The last patient admitted to the Children's Ward of the County Hospital last year was on October 9. Although this is November, we are still admitting patients with typhoid, and there are five or six cases reported in the city each day. The location of the epidemic is, so far as I am aware, principally on the south side. Every effort is being made to trace the infection. The water and crib have been thoroughly examined and the mains are perfect, so oysters and fish are under suspicion. There were 230 cases last year, of which 23.5 per cent. were in children, showing the importance of the subject from the pediatric standpoint. Thirty persons died from typhoid.

Last year we had nine cases of typhoid during the summer, beginning March 20, and ending October 9. This year we have had so far twenty-two cases of typhoid representing the same group, and the cases are still coming in. Those of you who remember back as far as I do will remember when typhoid was considered a serious disease in Chicago, and when recruits were asked from medical schools to come and do night nursing in the typhoid wards. He then spoke of the use of vaccine. We have a family in the hospital, with two cases out of six, in which all the other members were immediately protected against typhoid fever. The child who developed the fever second had received only the second dose when the disease developed. It does not seem to take as long to produce protection in typhoid as it does with the toxin-antitoxin. In these cases hemorrhage and perforation are rare, but in the last two years one case of hemorrhage occurred, and we have here a child with a number of relapses, to which I wish to call your attention.

The histories of these children, obtained from their parents, are almost identical. All complain of anorexia, of malaise and some diarrhea; occasionally they complain of chilliness, rarely of cough; last year there were some with nose bleed but so far this year there has been none. Sometimes a chilliness, but always the malaise, is the dominant feature attracting the parents' notice, Absolute diagnosis is dependent on two things, the leukopenia and the Widal test. Blood cultures have not been very successful but the Widal test is universally successful and with a very high titer in many cases. As corroborative evidence of typhoid incidence we have the fecal and urinary cultures, which always come back positive.

The length of stay in the hospital has averaged about four and a half weeks. Some were forced cases which had almost reached the convalescent stage when they were brought to the hospital, and were only in from twelve to fourteen days when the cultures became negative and they were sent out. Most cases come in at the beginning of the second week, so probably the average length of the disease is about six weeks. The history of one case has been very interesting.

L., a girl, aged 6 years, came into the hospital Oct. 19, 1923, with a history of cough, fever and diarrhea of two weeks' duration. Her stools had been liquid yellow, she had abdominal pain for one day and considerable malaise. The onset had been abrupt, with a chill. Examination showed numerous harsh râles in both lungs; a palpable spleen, and a white count of 4,200 with 2,720,000 reds. On October 22 the Widal test was positive, 1 to 1,280, and on the following day typhoid organisms were recovered from the stool and urine. Her tuberculin reaction was negative. A blood count ten days after entrance showed a white count of 4,800. The temperature curve, which is similar to that seen in the majority of our cases, was as follows: The first week showed 100 F. at the low point and 104.5 at the high point. The second week varied between 103 and 98. The third week ranged from 100 to 98. During the fourth week 100 F. was reached only once, the temperature remaining fairly constantly below

99. The diurnal range was a characteristic low point in the morning and high in the afternoon.

Most of the children do not come in this year with a history of bronchial irritation, as was the case last year. Many of the patients last year had to be differentiated from miliary tuberculosis or acute bronchitis with temperature.

The following is the history of another child whose case was rather puzzling:

A girl, aged 8 years, came into the hospital on June 23, 1923. She had a history of a temperature for one week but was not in good health the week before. There was loss of appetite, drowsiness, and a septic type of temperature from the beginning. Physical examination showed moist râles and a few subcrepitant and sonorous râles. Slight rigidity of the abdomen was present, accompanied by moderate tenderness. The first blood examination showed a white count of 7,500, 44 per cent. of which were lymphocytes, and a negative Pirquet test. The Widal test was positive. On June 26, three days after admission, the white count was 8,800. On July 10, typhoid organisms were obtained from the stool. The temperature during this time had a high range up to 104 F. during the first week. In the second week the temperature was 103 with a low point of 100. In the third week it did not drop below 102 at any time, and in the fourth week it ranged between 102 and 105. At this time the child had a moderate intestinal hemorrhage, with a poor pulse ranging from 160 to 180. The temperature dropped to 100 with this hemorrhage but rose to 102 the following day. Prior to this hemorrhage the pulse range was between 130 and 140. This was on July 19. On the following day there was a second hemorrhage, and the white blood count was 7,800, the hemoglobin 45 per cent., and the coagulation time two and one-half minutes. In the sixth week the temperature ranged below 99. In the seventh week there was a relapse, with the temperature reaching 105, with sharp peaks and drops to 100. The eighth week the curve ranged from 102 to 98, gradually falling to normal, when in the eleventh week the child was discharged well.

He presented a temperature chart of one patient with a prolonged temperature. The patient was still in the hospital, then in his tenth week. There had been several relapses but no other complications. The case resembled pulmonary tuberculosis, not only because of the constancy of the temperature with its rise and fall, but because there was very little swing in the temperature for some time and there were moist râles in the chest. At the time of the second relapse the temperature reached 105 and in the twelfth week the child had a temperature of 98 for the first time.

Regular Meeting, Dec. 18, 1923

H. W. Cheney, M.D., *President*

Congenital Absence of the Radius. Presented by Dr. Katsuji Kato (by invitation).

Congenital absence of the radius was once thought to be rare, but there are 250 recorded cases, showing approximately an equal occurrence of bilateral and unilateral defect. The absence of the bone is usually complete, only 12 per cent. being incomplete or rudimentary. The principal pathologic change is the absence of the radius which is of congenital origin, and the ulna is usually hypertrophied and curved, while the hand shows radiopalmar deviation. The absence of the thumb is rather a constant finding, while syndactylism and polydactylism are frequently associated. The associated pathology also includes one or more other congenital anomalies.

In this paper, three cases are reported from the orthopedic service of Dr. Edwin W. Ryerson, the Children's Memorial Hospital, Chicago.

Case 1.—J. P., a boy, Italian, showed complete bilater[illegible]sence of the radius. The left thumb was normal but the right attached loosely to the hand by means of a fibrous tissue and fell off two months later. The child finally succumbed to pneumonia at the age of 2 years.

Case 2.—F. K., a girl, American, was first seen in the Dispensary at the age of 2 months when the diagnosis of congenital absence of the right radius was made, on the strength of characteristic radiopalmar clubhand and transposition of the radial artery, which was later confirmed by roentgenologic evidences. At 6 years of age, Dr. Ryerson performed the operation on the affected limb when a bone graft was taken from the hypertrophied ulna and inserted into the radial site, the forearm subsequently being held in extension by a plaster cast.

Case 3.—B. S., a girl, American, showed partial absence of the radius, the upper fragment of the bone being normal. The later history of the patient is lacking as she failed to return for further observation and treatment.

The etiologic consideration of the defect is interesting although more or less theoretical. Of the more important theories, Gegenbauer's archipterygeal theory, Dareste's amniotic compression theory are worthy of thought, but none of them appear to be adequate. The author advances a theory of embryonic cellular dystrophy, which considers the defect as arising from cell anomalies which might have resulted from various factors, such as inherent vagaries of chromosome material, defective cytoplasm, trophic nerve disturbance, abnormal blood supply or some form of fetal or maternal inflammation, producing a veritable scar tissue which inhibits the normal development of the osteogenetic mesoderm.

The treatment is largely surgical. The prognosis is gloomy. In many cases the unfortunate victims die young because of the seriousness of associated anomalies. When they survive till childhood, they become an easy prey of intercurrent infection. The correction of the deformity depends on the degree of pathologic changes, but it can usually be remedied, although the deformed hand remains always weak and the affected extremity always atrophied.

This presentation was discussed by Drs. Grulee, Brennemann and Cheney.

The Intradermal Salt Solution Test. II. Its Prognostic Value in Cases of So-Called Nephritis with Generalized Edema. Presented by Drs. C. A. Aldrich and W. B. McClure.

In July 1923, a preliminary report on observations on the time required for the disappearance of intradermally injected salt solution was published. It was found that the elevation produced by the intracutaneous injection of 0.8 per cent. sodium chlorid solution disappeared much more rapidly in cases with edema than in a small group of controls. The technic is as follows:

Two-tenths cubic centimeter of an 0.8 per cent. aqueous solution of sodium chlorid is injected intracutaneously under aseptic conditions. Duplicate injections are made about 2 cm. apart, either in the forearm or in the leg, or in both. In the forearm the flexor surface is used, and in the leg, either the inner surface of the calf or the lateral side of the anterior surface of the leg. The needle is inserted sufficiently superficially so that the lumen is visible through the skin. The end point of the disappearance of the elevation can best be determined by palpation unassisted by inspection, since color changes seen about the point of injection may cause confusion. It is necessary to disregard the very small traumatic elevation that is occasionally produced just where the needle enters the skin. This may persist after the large elevation, due to the injected salt solution, has disappeared.

We have come to consider sixty minutes as a lower limit of the normal range.

This paper reports the observations made on fifteen cases with generalized edema and pathologic urinary findings without evidence of cardiovascular disease.

A summary of the observations shows:

1. In a general way the greater the edema the shorter was the absorption time and vice versa.

2. In all cases, where tests were made previous to the occurrence of edema, demonstrable by pitting, there was a reduction of the absorption time, days and sometimes even weeks, before pitting was demonstrable. The absorption time in improving edematous cases was increased before the edema showed any apparent decrease, in all cases tested at such opportune time. During improvement it has closely approached the lower normal limits before the pitting was entirely gone.

3. There was no constant relationship between the absorption time and the severity of the urinary findings.

4. There was a marked parallelism between the absorption time and the urinary output, although the change in the absorption time usually preceded the change shown on the urinary output chart.

5. Recovery sometimes occurred even when the absorption time was less than one minute. However, in every fatal case the absorption time in the leg fell below one minute.

6. During improvement with weight gain, the absorption time curve tended to parallel that of the weight. During changes of weight due to retention or loss of water, these curves were in opposite directions.

7. In three cases tested only during or after convalescence, the time was within the normal range.

Graphic charts of observations on five of these cases were shown, demonstrating the points given above.

Charts of two cases with cardiovascular disease, pathologic urinary findings and edema were shown in contrast.

We believe these results justify the following conclusions:

1. This test is a valuable means of determining the immediate prognosis in such cases, and shows changes at an earlier date than shown by any other means with which we are familiar.

2. It is an aid in directing the therapeutic management of these cases.

3. These results are confirmatory evidence in favor of the theories that the tissues in this type of case are active in the development of edema.

4. It may be of considerable value in differentiating between circulatory and "renal" types of edema.

DISCUSSION

DR. W. B. McCLURE: Dr. Aldrich mentioned the fact that we had found decreased absorption time after ether anesthesia. I wish to speak more in detail of our results in the study of these cases.

In a series of ten children receiving ether for surgical procedures, principally tonsil and adenoid operations, we found a reduction of the absorption time ranging from 81 to 24 per cent. following the anesthesia. This effect did not differ materially in the cases in which atropin was used and those in which it was not used. It is known that ether anesthesia produces a certain degree of acidosis. This acidosis may logically be the cause of the decreased absorption time, although the possibility of the participation of other toxic influences, due to the anesthesia, must be considered. This is of interest in connection with the case referred to by Dr. Aldrich where the tonsillectomy was done, through an error in interpretation of orders, at a time when slight pitting and a drop in the absorption time had indicated a beginning edema. The child developed a very marked edema following the anesthesia, which we thought might have been due, in part, to the anesthetic.

Dr. Jesse R. Gerstley: As I understand, the technic of the test is 0.2 of 1 c.c. May I ask just how accurately this must be measured? I should think that a difference of a few tenths of a cubic centimeter might not be very important in this connection.

Dr. Aldrich (in closing): As regards the amount of the solution injected, I do not think it makes a bit of difference exactly how much you use. As a matter of fact, in doing this test in some of the cases the needle, or syringe, leaks while we are injecting the solution and we find that one wheal is larger than the other when it is put in, but that they both disappear at the same time. Theoretically, it would not make any difference and practically we have found that to be true, but if one is to give any idea of the test it is necessary to have some knowledge of the approximate amount we are using.

Regarding the use of alkalis, I think many of their urines were not alkaline at the time of testing. We have put most of the patients on alkalis, however. In the number of things to be done that is one of the things that has not yet been investigated thoroughly, but it should be. Also, the question of salt intake and output should be studied. We have done one test recently to see whether various concentrations of salt would make any difference, figuring that if osmotic influences were predominating in edema, as some claim, if we put into the skin a solution of two or three times the salt concentration normally found in the body, the fluid should remain a long time in the skin. The disappearance of the wheals showed a difference of only one minute or so. We used three different strengths of salt, one 1.6, another 2.4, and another 3.2, the last being in excess of any concentration ever found in the body. That solution was absorbed almost as rapidly as the others. While that needs to be confirmed, I think it shows that the osmotic factors are not the predominant ones at work.

When we did this test at first it took a long time to figure out how long the wheal normally lasted. Because of some experiments on rabbits we thought that it disappeared within a few minutes. We kept on working and found sixty minutes which at first we thought was pretty high, but which we now consider a comparatively short time. The higher the time the better for the patient. We go to the patient without knowing where we have put the injection and if when we feel the arm or leg we discover the location of the wheal we know it is still present.

Regular Meeting, Feb. 19, 1924

H. W. Cheney, M.D., *President*

Concerning the Etiology of Hypertrophic Pyloric Stenosis. Presented by Dr. Louis W. Sauer, this issue p. 608.

DISCUSSION

Dr. Joseph Brenneman: I want to ask one question. Some years ago Hess of New York made a statement which in my opinion was not especially confirmed by evidence which he presented, that with a pyloric spasm there were other spasms in the intestinal tract, namely, cardiospasm, rectal sphincter spasm, and general hypertonicity of the whole intestinal tract. I wonder if that idea has received support elsewhere. There are two other conditions which I think closely simulate pylorospasm. I saw one such case in a child aged 2 weeks. The child had typical peristaltic waves, except that they did not point quite right, they pointed toward the navel instead of the liver. This proved to be a case of volvulus. The other condition, which I have seen twice, was duodenal obstruction. In each case the baby vomited quantities of bile, and this of course distinguished it from pyloric obstruction, in which this could not occur.

Dr. Clifford Grulee: Greenebaum observed a child operated on, aged 2 days. That would seem to be a case where it was a typical pyloric stenosis, and it would support the theory that it could be a congenital anomaly. Another condition associated with vomiting and also frequent is rumination. I have seen in this many times active peristalsis, in cases which were not true pyloric stenosis in the ordinary sense of the word.

Dr. Julius H. Hess: Has Dr. Sauer had occasion to study any fetal cases? I have sections of pyloruses taken from fetuses ranging from 18 to 28 weeks. All show a very well developed layer of circular and a thin longitudinal muscle, but even more striking is the marked infolding of the mucosa. In the fetus, the mucus membrane of the pylorus is very abundant and appears excessive when compared with cross section of older infants.

Is it not possible that the consequent infolding and compression of the mucosa may not act in such a manner as to cause repeated contraction of the circular muscle fibers resulting in gradual hypertrophy either in fetal or early extra uterine life?

Dr. Sauer (closing): I came across several articles in the literature which speak about this spasm of the entire intestinal canal. I spoke to Dr. Alvarex, who has written extensively on the intestinal canal, and he thought the condition was simply spastic. Professor Carlson thought if we studied the condition we would not find hypertrophy. We read so much about pyloric spasm, especially in American literature, but in the last few years Holt said the thing does not exist. He said these are mild and severe cases of hypertrophy.

Mohr has had two cases, which he published, of pure pyloric spasm which ran a long while and ended fatally, without hypertonia. He published a report on one of them, which he had followed for weeks, in great detail. Greenebaum had a typical case, operated on the second day. With regard to the fetal pylorus I have not done much, but a number of Danish and Norwegian anatomists have published wonderful works on this subject. The only ones who disagree with this work, that is, that the pylorus in the fetus may show a marked stenosis, are the English physicians. Cunningham and one or two others claim the muscle is thicker a few weeks after birth than during fetal life. But most of the work shows very defintely that in the fetus the muscularis is distinctly thicker.

Cell Counts in Bloody Spinal Fluid (Inaugural Thesis). H. E. Irish.

A detailed technic is presented for counting white cells in slightly bloody cerebrospinal fluid. Test counts are reported on ten fluids made by three counters for checking against each other and against a computed number of cells. The results shown are approximately correct in average from the standpoint of diagnostic usability. It is shown that accuracy was increased by promptness in counting. The use of this same technic by three counters in ten fluids showed an increase in accuracy of 133 per cent. in white blood cells and 8 per cent. in red blood cells, over five fluids counted by the two counters using their usual methods.

Slightly bloody fluids are shown to be usable diagnostically. The use of this technic where much blood is present or in purulent fluids is not discussed in this paper. Purulent fluids readily reveal their identity by their great increase in white cell content. Bloody spinal fluids are best counted immediately, but can be transported and counted within a few hours with approximate accuracy.

The technic used to count leukocytes in spinal fluid was as follows:

1. Draw stain (Wright's methylene blue 50 per cent., glacial acetic acid 50 per cent.) to Point 1 in white pipet.
2. Shake fluid thoroughly and draw up from its central portion to Point 11.
3. Rotate and shake pipet for one minute.
4. Let stand ten minutes for complete staining and decolorizing.
5. Shake again thoroughly, allow first few drops to escape from tube and then place drop in counting chamber.
6. Use low power to find counting lines, then high power to ascertain the effect of stain.
7. If whites are fully stained and reds are completely decolorized, use low power for counting.
8. If contrary is found, use high power for count.
9. Focus up and down on doubtfuls. Increased refractility decides identity of whites.
10. Count two full fields of 9 large squares (Levy ruling) on 16 (Thoma Zeiss).
11. Take average of two fields and multiply by 10/8.

To count erythrocytes in spinal fluid:

1. Shake fluid thoroughly, use drop from central portion to place on counting chamber.
2. Count 5 large squares (= 80 small squares) and multiply by 0.50.
3. If cells are too numerous to count in chamber, dilute with Hayem's solution and use proper multiplier.
4. The results of these tests are shown in tables.

DISCUSSION

Dr. Clifford G. Grulee pointed to the practical application of this paper.

Dr. Ray L. Critchfield: Recently at the Children's Hospital we have changed our method of collecting spinal fluid for the white cell count.

We now place 1 mm. of glacial acetic acid in a test tube and permit 9 drops of spinal fluid to fall into the tube directly from the needle. We find that the fluid stands up better and this method does not interfere with the accuracy of the count. All counts must be made within fifteen minutes from the time they are obtained, which we believe makes for greater accuracy.

Dr. Irish (in closing): Answering Dr. Grulee, the range of utility of the technic probably will be limited to fluids that have a cell count varying from 50 to 100. In that particular range of cell counts are tuberculosis, poliomyelitis, one form of syphilis, mild septic meningitis and the like. In this field, very often the number of cells in the spinal fluid is of great service in indicating the nature of the fluid. The increase would have to be calculated with great care in order to avoid being misled by it. In counts over 500 the white cells are usually sufficiently numerous so that a smear will show the nature of the fluid.

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PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $4.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

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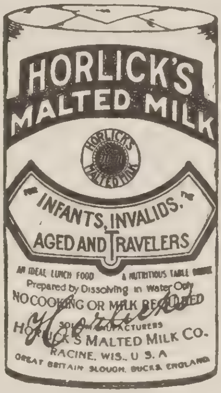
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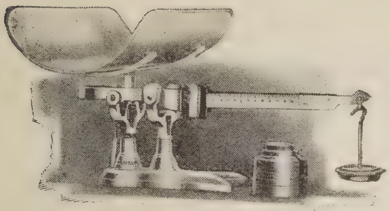

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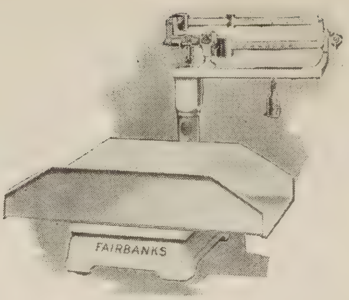

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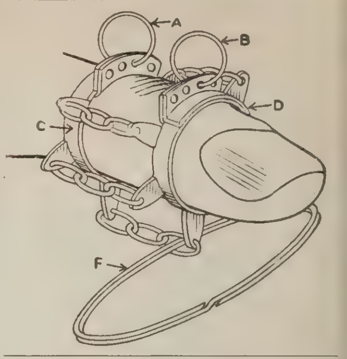

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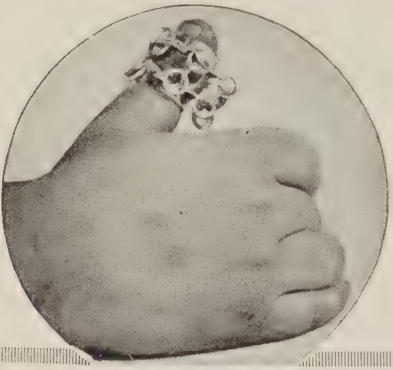

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Analysis (Dry)		Reliquefied 11 parts water and 1 part powder. (Approximating Finklestein's Formula)	
Protein	38%	Protein	3.16
Butterfat	27%	Butterfat	2.25
Lactose	24%	Lactose	2.00
Ash	5%	Ash	.42
Free Lactic Acid	3%	Free Lactic Acid	.25
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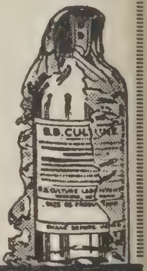

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ALBUMIN	5.46%	.65%
LACTOSE	38.00%	4.53%
ASH	5.76%	.69%
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CALORIES (*per ounce*)	149	18.

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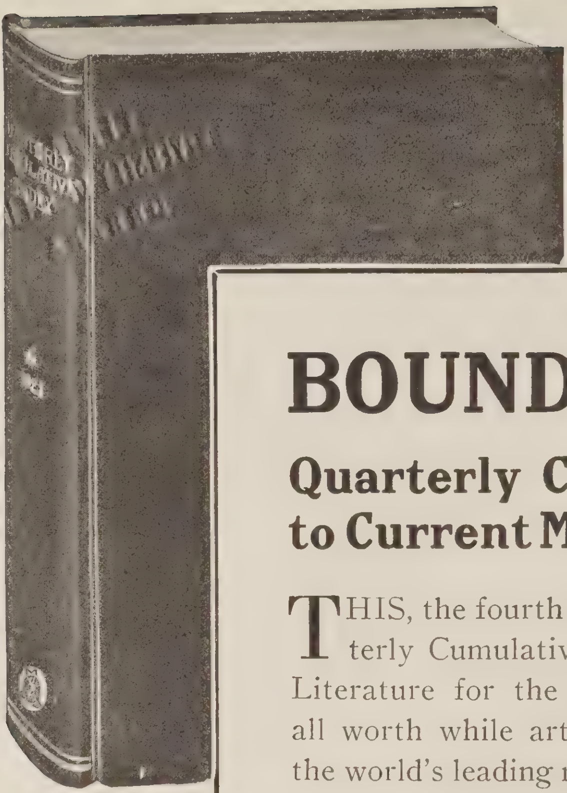

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